(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
10 April 2003 (10.04.2003)

PCT

(10) International Publication Number
WO 03/028641 A2

(51) International Patent Classification⁷: A61K

(21) International Application Number: PCT/US02/31059

(22) International Filing Date:
30 September 2002 (30.09.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/326,463 1 October 2001 (01.10.2001) US
60/326,758 2 October 2001 (02.10.2001) US

(71) Applicant *(for all designated States except US)*: **TAISHO PHARMACEUTICAL CO., LTD.** [JP/JP]; 24-1, Takata 3-chome, Toshima-ku, Tokyo 171-8633 (JP).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: **SEKIGUCHI, Yoshinori** [JP/JP]; 24-1, Takata 3-chome, Toshima-ku, Tokyo 171-8633 (JP). **KANUMA, Kosuke** [JP/JP]; 24-1, Takata 3-chome, Toshima-ku, Tokyo 171-8633 (JP). **OMODERA, Katsunori** [JP/JP]; 24-1, Takata 3-chome, Toshima-ku, Tokyo 171-8633 (JP). **TRAN, Thuy-Anh** [US/US]; 4833 Fairport way, San Diego, CA 92130 (US). **KRAMER, Bryan, Aubrey** [US/US]; 5645 Friars Road #358, San Diego, CA 92110 (US). **BEELEY, Nigel, Robert, Arnold** [GB/US]; 227 Loma Corta Drive, Solana Beach, CA 92705 (US).

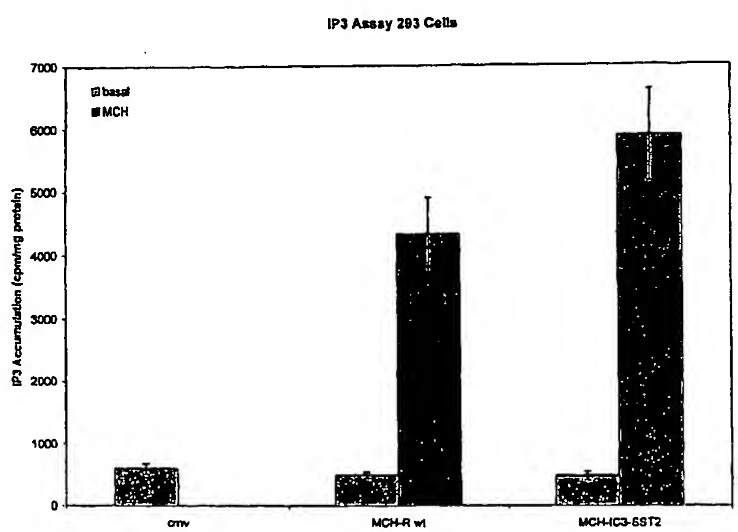
(74) Agents: **CORUZZI, Laura, A.** et al.; Pennie & Edmonds LLP, 1155 Avenue of the Americas, New York, NY 10036 (US).

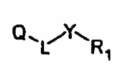
(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),

[Continued on next page]

(54) Title: MCH RECEPTOR ANTAGONISTS




(I)

(57) **Abstract:** The present invention relates to novel compounds of the formula (I) which act as MCH receptor antagonists. These compositions are useful in pharmaceutical compositions whose use includes prophylaxis or treatment of obesity, obesity related disorders, anxiety, or depression.

WO 03/028641 A2

Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

MCH RECEPTOR ANTAGONISTS

Field of the Invention

The present invention relates to compounds which act as antagonists for MCH receptors and to the use of these compounds in pharmaceutical compositions.

Background of the Invention

Melanin Concentrating Hormone (MCH), a cyclic peptide, has been identified as the endogenous ligand of the orphan G-protein coupled receptor SLC-1. See, for example, Shimomura et al., Biochem. Biophys. Res. Commun. 261, 622-26 (1999). Studies have indicated that MCH acts as a neurotransmitter/neuromodulator to alter a number of behavioral responses such as feeding habits. For example, injection of MCH into rats has been reported to increase their consumption of food. Reports indicate that genetically engineered mice which lack MCH show lower body weight and increased metabolism. See Saito et al., TEM, vol. 11, 299 (2000). As such, the literature suggests that discovery of MCH antagonists that interact with SCL-1 expressing cells will be useful in developing obesity treatments. See Shimomura et al., Biochem. Biophys. Res. Commun. 261, 622-26 (1999).

G protein-coupled receptors (GPCRs) share a common structural motif. All these receptors have seven sequences of between 22 to 24 hydrophobic amino acids that form seven alpha helices, each of which spans the membrane. The fourth and fifth transmembrane helices are joined on the extracellular side of the membrane by a strand of amino acids that forms a relatively large loop. Another larger loop, composed primarily of hydrophilic amino acids, joins transmembrane helices five and six on the intracellular side of the membrane. The carboxy terminus of the receptor lies intracellularly, and the amino terminus lies in the extracellular space. It is thought that the loop joining helices five and six,

as well as the carboxy terminus, interact with the G protein. Currently, Gq, Gs, Gi, and Go are G proteins that have been identified as possible proteins that interact with the receptor.

Under physiological conditions, GPCRs exist in the cell membrane in equilibrium between two different states or conformations: an "inactive" state and an "active" state. A receptor in an inactive state is unable to link to the intracellular transduction pathway to produce a biological response. Changing the receptor conformation to the active state allows linkage to the transduction pathway and produces a biological response.

A receptor may be stabilized in an active state by an endogenous ligand or an exogenous agonist ligand. Recent discoveries, including but not exclusively limited to, modifications to the amino acid sequence of the receptor, provide alternative mechanisms other than ligands to stabilize the active state conformation. These approaches effectively stabilize the receptor in an active state by simulating the effect of a ligand binding to the receptor. Stabilization by such ligand-independent approaches is termed "constitutive receptor activation." In contrast, antagonists can competitively bind to the receptor at the same site as agonists, but do not activate the intracellular response initiated by the active form of the receptor, and therefore inhibit the intracellular responses by agonists.

Certain 2-aminoquinazoline derivatives have been reported to be NPY antagonists which are said to be effective in the treatment of disorders and diseases associated with the NPY receptor subtype Y5. See PCT Patent Application 97/20823. Quinazoline derivatives have also been found to be useful by enhancing antitumor activity. See PCT Patent Application 92/07844.

Recently, our current knowledge of human obesity has advanced dramatically. Previously, obesity was viewed as an oppugnant behavior of inappropriate eating in the setting of appealing foods. Studies of animal models of obesity, biochemical alterations in both humans and animals, and the complex interactions of psychosocial and cultural factors that create receptiveness to human obesity indicate that this disease in humans is multifaceted and deeply entrenched in biologic systems. Thus, it is almost certain that obesity has multiple causes and that there are different types of obesity. Not only does MCHR1 antagonist have potent and durable anti-obesity effects in rodents, it has surprising antidepressant and anxiolytic properties as well (Borowsky et al., Nature Medicine, 8, 825-830, 2002). MCHR1 antagonists have been reported to show antidepressant and anxiolytic activities in rodent models such as social interaction, forced swimming test and ultrasonic

vocalization. These findings indicate that MCHR1 antagonists could be useful for treatment of obesity patients with multiple causes. Moreover, MCHR1 antagonists could be used to treat subjects not only with obesity, but also those with depression and anxiety. These advantages make it different from NPY receptor antagonists, with which anxiogenic-like activity may be expected, as NPY itself has anxiolytic-like effect.

Obesity is also regarded as a chronic disease and the possibly of long-term treatment is a concept that is receiving more attention. In this context, it is noteworthy that the depletion of MCH leads to hypophagia as well as leanness (Shimada et al., Nature, 396, 670-674, 1998). By contrast, NPY (Erickson et al., Nature, 381, 415-418, 1996), as well as the Y1 (Pedrazzini et al., Nature Medicine, 4, 722-726, 1998) and Y5 receptors (Marsh et al., Nature Medicine, 4, 718-721, 1998), disrupted mice maintained a stable body weight or rather became obese. Considering the above reports, MCHR1 antagonists may be more attractive than Y1 or Y5 receptor antagonists in terms of long-term treatment of obese patients.

An increasing number of children and adolescents are overweight. Although not all overweight children will necessarily become overweight adults, the growing occurrence of obesity in childhood is likely to be reflected in increasing obesity in adult years. The high prevalence of obesity in our adult population and the likelihood that the nation of the future will be even more obese demands a re-examination of the health implications of this disease. See, Health Implications of Obesity. NIH Consens. Statement Online 1985 Feb 11-13; 5(9):1-7.

"Clinical obesity" is a measurement of the excess body fat relative to lean body mass and is defined as a body weight more than 20% above the ideal body weight. Recent estimates suggest that 1 in 2 adults in the United States is clinically obese, an increase of more than 25% over the past decades. Flegal M.D. et al., 22 Int. *J. Obes. Relat. Metab. Disor.* 39 (1998). Both overweight conditions and clinical obesity are a major health concerns worldwide, in particular because clinical obesity is often accompanied by numerous complications, *i.e.,* hypertension and Type II diabetes, which in turn can cause coronary artery disease, stroke, late-stage complications of diabetes and premature death. (*See*, e.g., Nishina P.M. et al., 43 *Metab.* 554 (1994)).

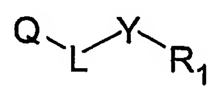
Although the etiologic mechanisms underlying obesity require further clarification, the net effect of such mechanisms leads to an imbalance between energy intake and

expenditure. Both genetic and environmental factors are likely to be involved in the pathogenesis of obesity. These include excess caloric intake, decreased physical activity, and metabolic and endocrine abnormalities.

Treatment of overweight conditions and clinical obesity via pharmaceutical agents are not only of importance with respect to the conditions themselves, but also with respect to the possibility of preventing other diseases that are associated with, *e.g.*, clinical obesity, as well as enhancement of the positive feeling of "self" that often accompanies those who are overweight or clinically obese and who encounter a significant reduction in body weight. Given the foregoing discussion, it is apparent that compounds which help in the treatment of such disorders would be useful and would provide an advance in both research and clinical medicine. The present invention is directed to these, as well as other, important ends.

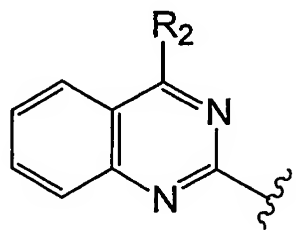
Summary of the Invention

The present invention, in one aspect, relates to compounds represented by Formula I:

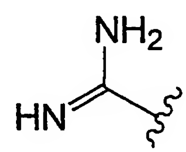


I

or a pharmaceutically acceptable salt or prodrug thereof, wherein Q is



or



II III

R_1 represents

(i) C_1-C_{16} alkyl,

C_1-C_{16} alkyl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•oxo,

•C_1-C_3 alkoxy,

•C_1-C_3 alkoxy substituted by substituent(s) independently selected from

••carbocyclic aryl,

••heterocyclyl,

••heterocyclyl substituted by C_1-C_3 alkyl,

•C_1-C_3 alkylcarbonyloxy,

•carbocyclyloxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by substituent(s) independently selected from

••halogen,

••nitro,

••carbocyclic aryl,

••carbocyclic aryl substituted by C_1-C_3 alkoxy,

••C_1-C_4 alkyl,

••C_1-C_4 alkyl substituted by substituent(s) independently selected from

•••oxo,

•••mono- or di-C_1-C_3 alkylamino,

•••mono- or di-C_1-C_3 alkylamino substituted by carbocyclic aryl,

•••mono- or di-C_1-C_3 alkylamino substituted by halogenated carbocyclic aryl,

•••carbocyclic arylcarbonylamino,

•••halogenated carbocyclic arylcarbonylamino,

•heterocyclyloxy,

•heterocyclyloxy substituted by C_1-C_3 alkyl,

•substituted heterocyclyl-ethylideneaminooxy,

•C_1-C_3 alkoxycarbonyl,

•C_1-C_3 alkoxycarbonyl substituted by carbocyclic aryl,

•mono- or di-C_1-C_3 alkylaminocarbonyl,

•mono- or di-C_1-C_3 alkylamino,

•mono- or di-C_1-C_3 alkylamino substituted by substituent(s) independently selected from

••cyano,

••carbocyclic aryl,

••heterocyclyl,

•mono- or di-carbocyclic arylamino,

•mono- or di-carbocyclic arylamino substituted by substituent(s) independently selected from

••hydroxy,

••C_1-C_3 alkyl,

•C_1-C_3 alkylcalbonylamino,

•C_1-C_3 alkylcalbonylamino substituted by substituent(s) independently selected from

••C_1-C_3 alkylcalbonylamino,

••carbocyclic arylcalbonylamino,

••heterocyclyl,

•C_1-C_4 alkoxycalbonylamino,

•heterocyclyl calbonylamino,

•carbocyclic arylsulfonylamino,

•carbocyclic arylsulfonylamino substituted by substituent(s) independently selected from

••nitro,

••C_1-C_3 alkyl,

••mono- or di-C_1-C_3 alkylamino,

•C_1-C_3 alkylthio,

•C_1-C_3 alkylthio substituted by substituent(s) independently selected from

••mono- or di-carbocyclic arylaminocarbonyl,

••halogenated mono- or di-carbocyclic arylaminocarbonyl,

••mono- or di-carbocyclic arylamino,

••halogenated mono- or di-carbocyclic arylamino,

••carbocyclic aryl,

••carbocyclic aryl substituted by substituent(s) independently selected from

•••halogen,

•••C_1-C_3 alkoxy,

•carbocyclic arylthio,

•carbocyclic arylthio substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

•carbocyclic arylsulfonyl,

•halogenated carbocyclic arylsulfonyl,

•heterocyclylthio,

•heterocyclylthio substituted by substituent(s) independently selected from

••nitro,

••C_1-C_3 alkyl,

•C_3-C_6 cycloalkyl,

•C_3-C_6 cycloalkyl substituted by C_1-C_3 alkyl,

•C_3-C_6 cycloalkenyl,

•carbocyclyl,

•carbocyclyl substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••C_2-C_3 alkenyl,

••C_2-C_3 alkenyl substituted by carbocyclic aryl,

••C_2-C_3 alkenyl substituted by carbocyclic aryl substituted C_1-C_3 alkylsulfinyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••nitro,

••C_1-C_4 alkyl,

••C_1-C_4 alkyl substituted by substituent(s) independently selected from

•••halogen,

•••hydroxy,

•••oxo,

•••carbocyclic aryl,

•••heterocyclyl,

•••mono- or di-carbocyclic arylamino,

•••mono- or di-carbocyclic arylamino substituted by substituent(s) independently selected from

••••halogen,

••••nitro,

••••C_1-C_3 alkyl,

••••C_1-C_3 alkoxy,

••••halogenated C_1-C_3 alkoxy,

••C_1-C_4 alkoxy,

••C_1-C_4 alkoxy substituted by substituent(s) independently selected from

•••halogen,

•••carbocyclic aryl,

••carbocyclic aryloxy,

••C_1-C_3 alkoxycarbonyl,

••C_1-C_3 alkylcarbonyloxy,

••mono- or di-C_1-C_3 alkylamino,

••mono- or di-carbocyclic arylamino,

••halogenated mono- or di-carbocyclic arylamino,

••mono- or di-carbocyclic arylaminocarbonyl,

••mono- or di-carbocyclic arylaminocarbonyl substituted by substituent(s) independently selected from

•••halogen,

•••nitro,

•••C_1-C_3 alkyl,

•••C_1-C_3 alkoxy,

•••halogenated C_1-C_3 alkoxy,

••mercapto,

••C_1-C_3 alkylthio,

••halogenated C_1-C_3 alkylthio,

••C_1-C_3 alkylsulfonyl,

••C_3-C_6 cycloalkyl,

••carbocyclic aryl,

••heterocyclyl,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••hydroxy,

••C_1-C_3 alkyl,

••C_1-C_3 alkyl substituted by carbocyclic aryl,

••C_1-C_3 alkoxy,

••C_1-C_3 alkoxy substituted by carbocyclic aryl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

(ii) C_2-C_8 alkenyl,

C_2-C_8 alkenyl substituted by substituent(s) independently selected from

•halogen,

•oxo,

•C_1-C_3 alkoxy,

•C_1-C_3 alkoxy substituted by carbocyclic aryl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••nitro,

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••halogenated C_1-C_3 alkoxy,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••hydroxy,

••nitro,

••C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

(iii) C_2-C_4 alkynyl,

C_2-C_4 alkynyl substituted by carbocyclic aryl,

(iv) C_3-C_6 cycloalkyl,

C_3-C_6 cycloalkyl substituted by substituent(s) independently selected from

•C_1-C_3 alkyl,

•C_1-C_3 alkyl substituted by substituent(s) independently selected from

••hydroxy,

••oxo,

••carbocyclic aryl,

•mono- or di-C_1-C_3 alkylamino,

•mono- or di-C_1-C_3 alkylamino substituted by carbocyclic aryl,

•carbocyclic arylcarbonylamino,

•carbocyclic aryl,

(v) C_3-C_6 cycloalkeyl,

C_3-C_6 cycloalkeyl substituted by C_1-C_3 alkyl,

(vi) carbocyclyl,

carbocyclyl substituted by substituent(s) independently selected from

•hydroxy,

•nitro,

(vii) carbocyclic aryl,

carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•cyano,

•nitro,

•C_1-C_9 alkyl,

•C_1-C_9 alkyl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••oxo,

••C_1-C_3 alkoxy,

••carbocyclic aryloxy,

••mono- or di-C_1-C_3 alkylamino-N-oxy,

••mono- or di-C_1-C_3 alkylamino,

••mono- or di-C_1-C_3 alkylamino substituted by carbocyclic aryl,

••mono- or di-carbocyclic arylamino,

••carbocyclylimino,

••carbocyclylimino substituted by carbocyclic aryl,

••mono- or di-carbocyclic arylamino,

••mono- or di-carbocyclic arylamino substituted by C_1-C_3 alkoxy,

••mono- or di-carbocyclic arylaminocarbonyl,

••mono- or di-carbocyclic arylaminocarbonyl substituted by C_1-C_3 alkoxy,

••carbocyclic aryl,

••carbocyclic aryl substituted by substituent(s) independently selected from

•••halogen,

•••C_1-C_3 alkyl,

•••halogenated C_1-C_3 alkyl,

••heterocyclyl,

••heterocyclyl substituted by C_1-C_3 alkyl,

•C_2-C_3 alkenyl,

•C_2-C_3 alkenyl substituted by carbocyclic aryl,

•C_1-C_9 alkoxy,

•C_1-C_9 alkoxy substituted by substituent(s) independently selected from

••hydroxy,

••halogen,

••carboxy,

••mono- or di-C_1-C_3 alkylamino,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

••heterocyclyl,

••heterocyclyl substituted by substituent(s) independently selected from

•••halogen,

•••heterocyclyl,

•••heterocyclyl substituted by substituent(s) independently selected from

••••halogen,

••••C_1-C_3 alkyl,

••••halogenated C_1-C_3 alkyl,

•C_2-C_3 alkenyloxy,

•C_1-C_3 alkylcarbonyloxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by substituent(s) independently selected from

••halogen,

••nitro,

••C_1-C_4 alkyl,

••halogenated C_1-C_4 alkyl,

••C_1-C_3 alkoxy,

•heterocyclyloxy,

•heterocyclyloxy substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl,

•(carbocyclic aryl)$S(O)_2O$,

•carboxy,

•C_1-C_3 alkoxycarbonyl,

•mono- or di-C_1-C_3 alkylaminocarbonyl,

•mono- or di-C_1-C_3 alkylaminocarbonyl substituted by carbocyclic aryl,

•mono- or di-carbocyclic arylaminocarbonyl,

•mono- or di-carbocyclic arylaminocarbonyl substituted by C_1-C_3 alkyl,

•amino,

•mono- or di-C_1-C_4 alkylamino,

•mono- or di-C_1-C_4 alkylamino substituted by cyano,

•mono- or di-carbocyclic arylamino,

•C_1-C_3 alkynylcarbonylamino,

•C_1-C_3 alkynylcarbonylamino substituted by carbocyclic aryl,

•carbocyclic arylsulfonylamino,

•carbocyclic arylsulfonylamino substituted by C_1-C_3 alkyl,

•(carbocyclic aryl)NHC(O)NH,

•(carbocyclic aryl)NHC(O)NH substituted by C_1-C_3 alkoxy,

•(carbocyclic aryl)NHC(O)NH substituted by haloganated C_1-C_3 alkoxy,

•carbocyclic aryl diazo,

•carbocyclic aryl diazo substituted by mono- or di- C_1-C_3 alkylamino,

•C_1-C_3 alkylthio,

•halogenated C_1-C_3 alkylthio,

•carbocyclic arylthio,

•carbocyclic arylthio substituted by substituent(s) independently selected from

••halogen,

••cyano,

••C_1-C_3 alkyl,

•heterocyclylthio,

•C_1-C_3 alkylsulfonyl,

•mono- or di-C_1-C_3 alkylaminosulfonyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••C_1-C_7 alkyl,

••halogenated C_1-C_7 alkyl,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••C_1-C_3 alkyl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

(viii) heterocyclyl,

or heterocyclyl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•cyano,

•nitro,

•C_1-C_4 alkyl,

•C_1-C_4 alkyl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••oxo,

••C_1-C_3 alkylcarbonyloxy,

••carbocyclic arylcarbonylamino,

••halogenated carbocyclic arylcarbonylamino,

••C_1-C_3 alkoxycarbonyl,

••C_1-C_3 alkylthio,

••C_1-C_3 alkylthio substituted by carbocyclic aryl,

••C_1-C_3 alkylthio substituted by halogenated carbocyclic aryl,

••carbocyclic aryl,

••carbocyclic aryl substituted by substituent(s) independently selected from

•••halogen,

•••nitro,

••heterocyclyl,

••heterocyclyl substituted by substituent(s) independently selected from

•••halogen,

•••C_1-C_3 alkyl,

•••halogenated C_1-C_3 alkyl,

•C_1-C_3 alkoxy,

•C_1-C_3 alkoxy substituted by carbocyclic aryl,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

•mono- or di-C_1-C_3 alkylamino,

•C_1-C_4 alkylcarbonylamino,

•C_1-C_3 alkylthio,

•C_1-C_3 alkenylthio,

•carbocyclic arylthio,

•halogenated carbocyclic arylthio,

•carbocyclic arylthio substituted by C_1-C_3 alkoxycarbonyl,

•heterocyclylthio,

•heterocyclylthio substituted by C_1-C_3 alkyl,

•C_1-C_3 alkylsulfonyl,

•carbocyclic arylsulfonyl,

•halogenated carbocyclic arylsulfonyl,

•carbocyclic arylsulfonyl substituted by C_1-C_4 alkyl,

•C_1-C_3 alkoxycarbonyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••nitro,

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••halogenated C_1-C_3 alkoxy,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••C_1-C_3 alkoxycarbonyl;

R_2 is $-NHNH_2$, -NHNHBoc, $-N(R_{2a})(R_{2b})$, morpholino, 4-acetyl-piperazyl, or 4-phenyl-piperazyl;

wherein R_{2a} is H or C_1-C_3 alkyl;

R_{2b} is C_1-C_4 alkyl, C_1-C_4 alkyl substituted by substituent(s) independently selected from

•hydroxy,

•C_1-C_3 alkoxy,

•amino,

•-NHBoc,

•C_3-C_6 cycloalkyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••$-SO_2NH_2$,

•heterocyclyl,

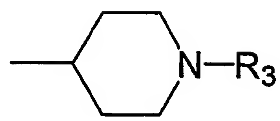
C_3-C_6 cycloalkyl, carbocyclic aryl, carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•C_1-C_3 alkyl,

•C_1-C_3 alkoxy,

or a group of Formula IV;



IV

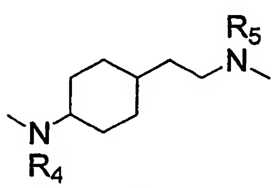
wherein Boc is carbamic acid *tert*-butyl ester and R_3 is C_1-C_3 alkyl or C_1-C_3 alkyl substituted by substituent(s) independently selected from

•carbocyclic aryl,

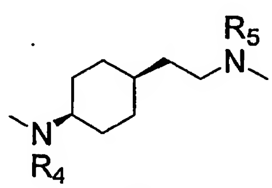
•halogenated carbocyclic aryl,

•carbocyclic aryl substituted by C_1-C_3 alkoxy;

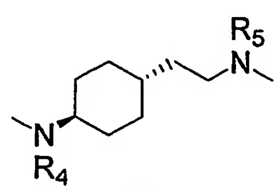
L is selected from Formula V - XIX;



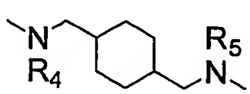
V



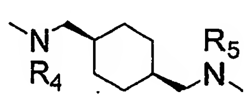
Va



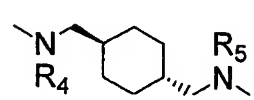
Vb



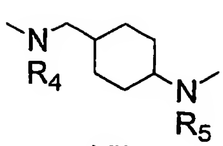
VI



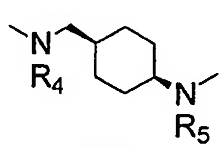
VIa



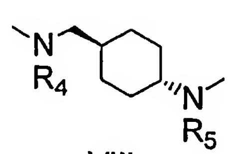
VIb



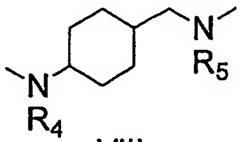
VII

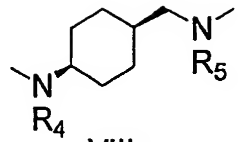


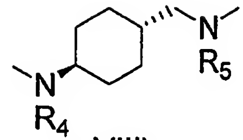
VIIa

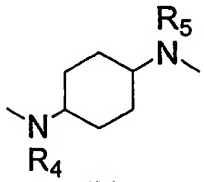


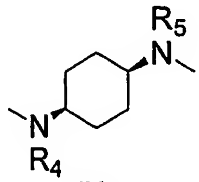
VIIb

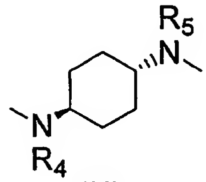

VIII

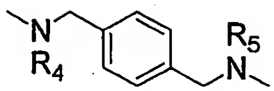

VIIIa

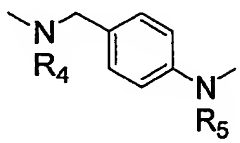

VIIIb

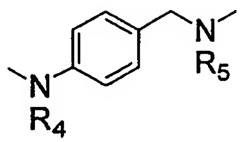

IX

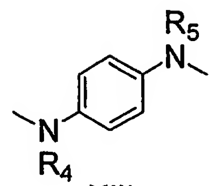

IXa

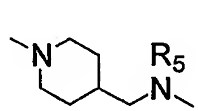

IXb

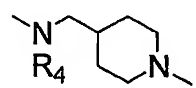

X

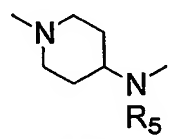

XI

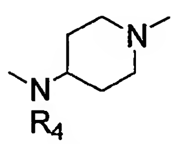

XII

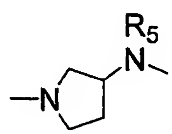

XIII

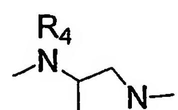

XIV


XV


XVI


XVII


XVIII


XIX

wherein R_4 is H or C_1-C_3 alkyl;

R_5 is H, C_1-C_3 alkyl, or C_1-C_3 alkyl substituted by a substituted carbocyclic aryl;

Y is $-S(O)_2-$, -C(O)-, or $-(CH_2)_m$;

m is 0 or 1;

wherein carbocyclic aryl is phenyl, naphthyl, anthranyl, biphenyl, or phenanthryl;

carbocyclyl is 10,11-dihydro-5-oxo-dibenzo[a,d]cycloheptyl, 1-oxo-indanyl, 7,7-

dimethyl-2-oxo-bicyclo[2.2.1]heptyl, 9*H*-fluorenyl, 9-oxo-fluorenyl, acenaphthyl, anthraquinonyl, *C*-fluoren-9-ylidene, indanyl, indenyl, 1,2,3,4-tetrahydro-naphthyl, or bicyclo[2.2.1]hepteny;

heterocyclyl is 1,2,3,4-tetrahydro-isoquinolyl, 1,2,3-thiadiazolyl, 1,2,3-triazolyl, 1,2-dihydro-3-oxo-pyrazolyl, 1,3,4-thiadiazolyl, 1,3-dioxo-isoindolyl, 1,3-dioxolanyl, 1*H*-indolyl, 1*H*-pyrrolo[2;3-c]pyridyl, 1*H*-pyrrolyl, 1-oxo-3*H*-isobenzofuranyl, 2,2',5',2"-terthiophenyl, 2,2'-bithiophenyl, 2,3-dihydro-1-oxo-isoindolyl, 2,3-dihydro-benzo[1,4]dioxinyl, 2,3-dihydro-benzofuryl, 2,4-dihydro-3-oxo-pyrazolyl, 2*H*-benzopyranyl, 2-oxo-benzopyranyl, 2-oxo-pyrrolidinyl, 3,4-dihydro-2*H*-benzo[1,4]oxazinyl, 3,4-dihydro-2*H*-benzo[b][1,4]dioxepinyl, 4*H*-benzo[1,3]dioxinyl, 4*H*-benzopyranyl, 4-oxo-1,5,6,7-tetrahydro-indolyl, 4-oxo-3,4-dihydro-phthalazinyl, 4-oxo-benzopyranyl, 9,10,10-trioxo-thioxanthenyl, 9*H*-carbazolyl, 9*H*-xanthenyl, azetidinyl, benzimidazolyl, benzo[1,3]dioxolyl, benzo[2,1,3]oxadiazolyl, benzo[b]thienyl, benzofuryl, benzothiazolyl, cinnolyl, furyl, imidazo[2,1-b]thiazolyl, imidazolyl, isoxazolyl, morpholino, morpholinyl, oxazolyl, oxolanyl, piperazyl, piperidyl, piridyl, pyrazolo[5,1-b]thiazolyl, pyrazolyl, pyridyl, pyrimidyl, pyrrolidyl, quinolyl, quinoxalyl, thiazolidyl, thiazolyl, thienyl, thiolanyl, 2,3-dihydro-benzofuryl, tetrahydro-thienyl, or benzofuranyl;

halogen is fluoro, chloro, bromo, or iodo.

Preferred compounds of this invention are those compounds of Formula I wherein,

Q is Formula II;

R_1 represents

(i) C_1-C_{10} alkyl,

C_1-C_{10} alkyl substituted by substituent(s) independently selected from

•halogen,

•oxo,

•C_1-C_3 alkoxy,

•C_1-C_3 alkoxy substituted by carbocyclic aryl,

•C_1-C_3 alkylcarbonyloxy,

•carbocyclyloxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by substituent(s) independently selected from

••halogen,

••nitro,

••C_1-C_4 alkyl,

••C_1-C_4 alkyl substituted by substituent(s) independently selected from

•••oxo,

•••carbocyclic arylcarbonylamino,

•••halogenated carbocyclic arylcarbonylamino,

•heterocyclyloxy,

•heterocyclyloxy substituted by C_1-C_3 alkyl,

•substituted heterocyclyl-ethylideneaminooxy,

•C_1-C_3 alkoxycarbonyl,

•C_1-C_3 alkoxycarbonyl substituted by carbocyclic aryl,

•mono- or di-C_1-C_3 alkylaminocarbonyl,

•mono- or di-carbocyclic arylamino,

•mono- or di-carbocyclic arylamino substituted by hydroxy,

•C_1-C_3 alkylcalbonylamino,

•C_1-C_3 alkylcalbonylamino substituted by substituent(s) independently selected from

••C_1-C_3 alkylcalbonylamino,

••carbocyclic arylcalbonylamino,

••heterocyclyl,

•C_1-C_4 alkoxycalbonylamino,

•heterocyclyl calbonylamino,

•carbocyclic arylsulfonylamino,

•carbocyclic arylsulfonylamino substituted by substituent(s) independently selected from

••nitro,

••C_1-C_3 alkyl,

••mono- or di-C_1-C_3 alkylamino,

•C_1-C_3 alkylthio,

•C_1-C_3 alkylthio substituted by substituent(s) independently selected from

••mono- or di-carbocyclic arylaminocarbonyl,

••halogenated mono- or di-carbocyclic arylaminocarbonyl,

••carbocyclic aryl,

••carbocyclic aryl substituted by substituent(s) independently selected from

•••halogen,

•••C_1-C_3 alkoxy,

•carbocyclic arylthio,

•carbocyclic arylthio substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

•carbocyclic arylsulfonyl,

•halogenated carbocyclic arylsulfonyl,

•heterocyclylthio,

•heterocyclylthio substituted by substituent(s) independently selected from

••nitro,

••C_1-C_3 alkyl,

•C_3-C_6 cycloalkyl,

•C_3-C_6 cycloalkyl substituted by C_1-C_3 alkyl,

•C_3-C_6 cycloalkenyl,

•carbocyclyl,

•carbocyclyl substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••C_2-C_3 alkenyl,

••C_2-C_3 alkenyl substituted by carbocyclic aryl,

••C_2-C_3 alkenyl substituted by carbocyclic aryl substituted C_1-C_3 alkylsulfinyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••nitro,

••C_1-C_4 alkyl,

••C_1-C_4 alkyl substituted by substituent(s) independently selected from

•••oxo,

•••carbocyclic aryl,

•••heterocyclyl,

••C_1-C_4 alkoxy,

••C_1-C_4 alkoxy substituted by substituent(s) independently selected from

•••halogen,

•••carbocyclic aryl,

••carbocyclic aryloxy,

••C_1-C_3 alkylcarbonyloxy,

••mono- or di-carbocyclic arylamino,

••halogenated mono- or di-carbocyclic arylamino,

••mono- or di-carbocyclic arylaminocarbonyl,

••mono- or di-carbocyclic arylaminocarbonyl substituted by substituent(s) independently selected from

•••halogen,

•••nitro,

•••C_1-C_3 alkyl,

•••C_1-C_3 alkoxy,

•••halogenated C_1-C_3 alkoxy,

••mercapto,

••C_1-C_3 alkylthio,

••halogenated C_1-C_3 alkylthio,

••C_1-C_3 alkylsulfonyl,

••C_3-C_6 cycloalkyl,

••carbocyclic aryl,

••heterocyclyl,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••hydroxy,

••C_1-C_3 alkyl,

••C_1-C_3 alkyl substituted by carbocyclic aryl,

••C_1-C_3 alkoxy,

••C_1-C_3 alkoxy substituted by carbocyclic aryl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

(ii) C_2-C_6 alkenyl,

C_2-C_6 alkenyl substituted by substituent(s) independently selected from

•oxo,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••nitro,

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••halogenated C_1-C_3 alkoxy,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••hydroxy,

••C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

(iii) C_3-C_6 cycloalkyl,

C_3-C_6 cycloalkyl substituted by substituent(s) independently selected from

•C_1-C_3 alkyl,

•C_1-C_3 alkyl substituted by substituent(s) independently selected from

••oxo,

••carbocyclic aryl,

•carbocyclic arylcarbonylamino,

•carbocyclic aryl,

(iv) carbocyclyl,

carbocyclyl substituted by nitro,

(v) carbocyclic aryl,

carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•cyano,

•nitro,

•C_1-C_9 alkyl,

•C_1-C_9 alkyl substituted by substituent(s) independently selected from

••halogen,

••oxo,

••carbocyclic aryloxy,

••carbocyclylimino,

••carbocyclylimino substituted by carbocyclic aryl,

••mono- or di-carbocyclic arylaminocarbonyl,

••mono- or di-carbocyclic arylaminocarbonyl substituted by C_1-C_3 alkoxy,

••carbocyclic aryl,

••carbocyclic aryl substituted by substituent(s) independently selected from

•••halogen,

•••C_1-C_3 alkyl,

•••halogenated C_1-C_3 alkyl,

••heterocyclyl,

••heterocyclyl substituted by C_1-C_3 alkyl,

•C_1-C_7 alkoxy,

•C_1-C_7 alkoxy substituted by substituent(s) independently selected from

••halogen,

••carbocyclic aryl,

•C_1-C_3 alkylcarbonyloxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by C_1-C_3 alkoxy,

•C_1-C_3 alkoxycarbonyl,

•mono- or di-C_1-C_3 alkylaminocarbonyl,

•mono- or di-C_1-C_3 alkylaminocarbonyl substituted by carbocyclic aryl,

•mono- or di-carbocyclic arylaminocarbonyl,

•mono- or di-carbocyclic arylaminocarbonyl substituted by C_1-C_3 alkyl,

•amino,

•mono- or di-C_1-C_3 alkylamino,

•C_1-C_3 alkynylcarbonylamino,

•C_1-C_3 alkynylcarbonylamino substituted by carbocyclic aryl,

•carbocyclic arylsulfonylamino,

•carbocyclic arylsulfonylamino substituted by C_1-C_3 alkyl,

•(carbocyclic aryl)NHC(O)NH,

•(carbocyclic aryl)NHC(O)NH substituted by C_1-C_3 alkoxy,

•(carbocyclic aryl)NHC(O)NH substituted by haloganated C_1-C_3 alkoxy,

•C_1-C_3 alkylthio,

•halogenated C_1-C_3 alkylthio,

•carbocyclic arylthio,

•carbocyclic arylthio substituted by cyano,

•C_1-C_3 alkylsulfonyl,

•mono- or di-C_1-C_3 alkylaminosulfonyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••C_1-C_7 alkyl,

••halogenated C_1-C_7 alkyl,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••C_1-C_3 alkyl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

(vi) heterocyclyl,

or heterocyclyl substituted by substituent(s) independently selected from

•halogen,

•nitro,

•C_1-C_4 alkyl,

•C_1-C_4 alkyl substituted by substituent(s) independently selected from

••halogen,

••oxo,

••C_1-C_3 alkylthio,

••C_1-C_3 alkylthio substituted by carbocyclic aryl,

••C_1-C_3 alkylthio substituted by halogenated carbocyclic aryl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

••heterocyclyl,

•C_1-C_3 alkoxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

•C_1-C_3 alkylthio,

•C_1-C_3 alkenylthio,

•carbocyclic arylthio,

•C_1-C_3 alkylsulfonyl,

•carbocyclic arylsulfonyl,

•halogenated carbocyclic arylsulfonyl,

•carbocyclic arylsulfonyl substituted by C_1-C_4 alkyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••nitro,

••C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl;

R_2 is -$NHNH_2$, -NHNHBoc, -$N(R_{2a})(R_{2b})$, morpholino, 4-acetyl-piperazyl, or 4-phenyl-piperazyl;

wherein R_{2a} is H or C_1-C_3 alkyl;

R_{2b} is C_1-C_4 alkyl, C_1-C_4 alkyl substituted by substituent(s) independently selected from

•hydroxy,

•C_1-C_3 alkoxy,

•amino,

•-NHBoc,

•C_3-C_6 cycloalkyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••-SO_2NH_2,

•heterocyclyl,

C_3-C_6 cycloalkyl, carbocyclic aryl, carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•C_1-C_3 alkyl,

•C_1-C_3 alkoxy,

or a group of Formula IV;

wherein Boc is carbamic acid *tert*-butyl ester and R_3 is C_1-C_3 alkyl or C_1-C_3 alkyl substituted by substituent(s) independently selected from

•carbocyclic aryl,

•halogenated carbocyclic aryl,

•carbocyclic aryl substituted by C_1-C_3 alkoxy;

L is selected from Formula V - XIX;

wherein R_4 is H or C_1-C_3 alkyl;

R_5 is H, C_1-C_3 alkyl, or C_1-C_3 alkyl substituted by a substituted carbocyclic aryl;

Y is -C(O)-;

wherein carbocyclic aryl is phenyl, naphthyl, anthranyl, or biphenyl;

carbocyclyl is 10,11-dihydro-5-oxo-dibenzo[a,d]cycloheptyl, 1-oxo-indanyl, 9*H*-fluorenyl, 9-oxo-fluorenyl, acenaphthyl, anthraquinonyl, *C*-fluoren-9-ylidene, indanyl, indenyl, 1,2,3,4-tetrahydro-naphthyl, or bicyclo[2.2.1]hepteny;

heterocyclyl is 1,2,3-thiadiazolyl, 1,2,3-triazolyl, 1,2-dihydro-3-oxo-pyrazolyl, 1,3-dioxo-isoindolyl, 1*H*-indolyl, 1*H*-pyrrolyl, 1-oxo-3*H*-isobenzofuranyl, 2,3-dihydro-benzo[1,4]dioxinyl, 2,3-dihydro-benzofuryl, 2,4-dihydro-3-oxo-pyrazolyl, 2*H*-

benzopyranyl, 2-oxo-benzopyranyl, 2-oxo-pyrrolidinyl, 3,4-dihydro-2*H*-benzo[b][1,4]dioxepinyl, 4-oxo-1,5,6,7-tetrahydro-indolyl, 4-oxo-3,4-dihydro-phthalazinyl, 4-oxo-benzopyranyl, 9,10,10-trioxo-thioxanthenyl, 9*H*-xanthenyl, azetidinyl, benzimidazolyl, benzo[1,3]dioxolyl, benzo[2,1,3]oxadiazolyl, benzo[b]thienyl, cinnolyl, furyl, imidazolyl, isoxazolyl, morpholino, morpholinyl, oxazolyl, oxolanyl, piperidyl, piridyl, pyrazolyl, pyridyl, pyrimidyl, pyrrolidyl, quinolyl, quinoxalyl, thiazolidyl, thiazolyl, thienyl, thiolanyl, tetrahydro-thienyl, benzofuranyl, or benzothiazolyl;

halogen is fluoro, chloro, bromo, or iodo.

Other preferred compounds of this invention are those compounds of Formula I wherein,

Q is Formula II;

R_1 represents

(i) C_1-C_{10} alkyl,

C_1-C_{10} alkyl substituted by substituent(s) independently selected from

•oxo,

•di-propylaminocarbonyl,

•methoxy substituted by carbocyclic aryl,

•methylcarbonyloxy,

•carbocyclic aryloxy,

•halogenated carbocyclic aryloxy,

•carbocyclic aryloxy substituted by nitro,

•heterocyclyloxy substituted by methyl,

•substituted heterocyclyl-ethylideneaminooxy,

•*tert*-butoxycarbonylamino,

•carbocyclic arylcarbonylamino,

•C_1-C_2 alkylthio,

•C_1-C_2 alkylthio substituted by substituent(s) independently selected from

••halogenated carbocyclic aryl,

••carbocyclic aryl substituted by methoxy,

•carbocyclic arylthio,

•hetrocyclylthio substituted by nitro,

•hetrocyclylthio substituted by methyl,

•C_5-C_6 cycloalkyl,

•C_5-C_6 cycloalkenyl,

•carbocyclyl substituted by substituent(s) independently selected from

••halogen,

••methyl,

••methoxy,

••ethenyl substituted by carbocyclic aryl substituted methylsulfinyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••nitro,

••C_1-C_4 alkyl,

••C_1-C_4 alkyl substituted by substituent(s) independently selected from

•••oxo,

•••carbocyclic aryl,

•••heterocyclyl,

••C_1-C_4 alkoxy,

••halogenated C_1-C_4 alkoxy,

••C_1-C_4 alkoxy substituted by carbocyclic aryl,

••carbocyclic aryloxy,

••halogenated mono-carbocyclic arylaminocarbonyl,

••carbocyclic aryl,

••heterocyclyl,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••C_1-C_2 alkyl,

•• C_1-C_2 substituted by carbocyclic aryl,

••methoxy,

••methoxy substituted by carbocyclic aryl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

(ii) C_2-C_3 alkenyl substituted by substituent(s) independently selected from

•carbocyclic aryl,

•halogenated carbocyclic aryl,

•carbocyclic aryl substituted by nitro,

(iii) C_3-C_6 cycloalkyl,

C_3-C_6 cycloalkyl substituted by substituent(s) independently selected from

•methyl substituted by oxo,

•methyl substituted by carbocyclic aryl,

•carbocyclic aryl,

(iv) carbocyclyl,

(v) carbocyclic aryl,

carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•cyano,

•nitro,

•C_1-C_9 alkyl,

•C_1-C_9 alkyl substituted by substituent(s) independently selected from

••halogen,

••oxo,

••carbocyclic aryl,

••carbocyclic aryl substituted by methyl,

••carbocyclic aryloxy,

•C_1-C_7 alkoxy,

•halogenated C_1-C_7 alkoxy,

•C_1-C_7 alkoxy substituted by carbocyclic aryl,

•methylcarbonyloxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by methoxy,

•amino,

•di-methylamino,

•propargynylcarbonylamino substituted by carbocyclic aryl,

•carbocyclic arylsulfonylamino substituted by methyl,

•(carbocyclic aryl)NHC(O)NH substituted by halogenated methoxy,

•halogenated methylthio,

•carbocyclic arylthio substituted by cyano,

•di-propylamino sulfonyl,

•mono- or di- ethylaminocarbonyl substituted by carbocyclic aryl,

•carbocyclic aryl,

•heterocyclyl substituted by methyl,

•heterocyclyl substituted by halogenated carbocyclic aryl,

(vi) heterocyclyl,

or heterocyclyl substituted by substituent(s) independently selected from

•halogen,

•nitro,

•C_1-C_4 alkyl,

•C_1-C_4 alkyl substituted by substituent(s) independently selected from

••halogen,

••methylthio substituted by halogenated carbocyclic aryl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

••heterocyclyl,

•methoxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by methyl,

•C_1-C_3 alkylthio,

•propenylthio,

•carbocyclic arylthio,

•C_1-C_3 alkylsulfonyl,

•carbocyclic arylsulfonyl substituted by C_1-C_4 alkyl,

•carbocyclic aryl,

•halogenated carbocyclic aryl,

•carbocyclic aryl substituted by methyl,

•carbocyclic aryl substituted by nitro,

•heterocyclyl;

R_2 is methylamino or dimethylamino;

L is selected from Formula Va, VIIIa, or IXa;

wherein R_4 and R_5 are independently selected from H or C_1-C_3 alkyl;

Y is -C(O)-;

wherein carbocyclic aryl is phenyl, naphthyl, anthranyl, or biphenyl;

carbocyclyl is 1-oxo-indanyl, 9-oxo-fluorenyl, indenyl, anthraquinonyl, *C*-fluoren-9-ylidene, 1,2,3,4-tetrahydro-naphthyl, or bicyclo[2.2.1]hepteny;

heterocyclyl is 1,2,3-thiadiazolyl, 1,2,3-triazolyl, 1,2-dihydro-3-oxo-pyrazolyl, 1,3-dioxo-isoindolyl, 1*H*-indolyl, 1*H*-pyrrolyl, 1-oxo-3*H*-isobenzofuranyl, 2,3-dihydro-benzo[1,4]dioxinyl, 2,4-dihydro-3-oxo-pyrazolyl, 2*H*-benzopyranyl, 2-oxo-benzopyranyl, 3,4-dihydro-2*H*-benzo[b][1,4]dioxepinyl, 4-oxo-3,4-dihydro-phthalazinyl, 4-oxo-benzopyranyl, 9,10,10-trioxo-thioxanthenyl, 9*H*-xanthenyl, azetidinyl, benzimidazolyl, benzo[1,3]dioxolyl, benzo[2,1,3]oxadiazolyl, benzo[b]thienyl, furyl, imidazolyl, isoxazolyl, morpholino, morpholinyl, oxolanyl, piperidyl, piridyl, pyrazolyl, pyridyl, quinolyl, quinoxalyl, thiazolidyl, thiazolyl, thienyl, thiolanyl, 2,3-dihydro-1-oxo-isoindolyl, 2,3-dihydro-benzofuryl, 2-oxo-pyrrolidinyl, 4-oxo-1,5,6,7-tetrahydro-indolyl, cinnolyl, pyrimidyl, pyrrolidyl, tetrahydro-thienyl, benzofuranyl, or benzothiazolyl;

halogen is fluoro, chloro, bromo, or iodo.

Other more preferred compounds of this invention are those compounds of Formula I wherein,

Q is Formula II;

R_1 represents

(i) C_1-C_{10} alkyl substituted by substituent(s) independently selected from

•oxo,

•di-propylaminocarbonyl,

•methoxy substituted by carbocyclic aryl,

•methylcarbonyloxy,

•carbocyclic aryloxy,

•halogenated carbocyclic aryloxy,

•carbocyclic aryloxy substituted by nitro,

•heterocyclyloxy substituted by methyl,

•*tert*-butoxycarbonylamino,

•carbocyclic arylcarbonylamino,

•C_1-C_2 alkylthio,

•C_1-C_2 alkylthio substituted by substituent(s) independently selected from

••halogenated carbocyclic aryl,

••carbocyclic aryl substituted by methoxy,

•carbocyclic arylthio,

•hetrocyclylthio substituted by nitro,

•hetrocyclylthio substituted by methyl,

•C_5-C_6 cycloalkenyl,

•carbocyclyl substituted by substituent(s) independently selected from

••halogen,

••methyl,

••methoxy,

••ethenyl substituted by carbocyclic aryl substituted methylsulfinyl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••nitro,

••C_1-C_4 alkyl,

••C_1-C_4 alkyl substituted by substituent(s) independently selected from

•••oxo,

•••carbocyclic aryl,

•••heterocyclyl,

••C_1-C_4 alkoxy,

••halogenated C_1-C_4 alkoxy,

••C_1-C_4 alkoxy substituted by carbocyclic aryl,

••carbocyclic aryloxy,

••halogenated mono-carbocyclic arylaminocarbonyl,

••carbocyclic aryl,

••heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••C_1-C_2 alkyl,

•• C_1-C_2 substituted by carbocyclic aryl,

••methoxy,

••methoxy substituted by carbocyclic aryl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

(ii) C_2-C_3 alkenyl substituted by substituent(s) independently selected from

•carbocyclic aryl,

•halogenated carbocyclic aryl,

•carbocyclic aryl substituted by nitro,

(iii) C_3-C_6 cycloalkyl substituted by substituent(s) independently selected from

•methyl substituted by oxo,

•methyl substituted by carbocyclic aryl,

•carbocyclic aryl,

(iv) carbocyclyl,

(v) carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•cyano,

•nitro,

•C_1-C_9 alkyl,

•C_1-C_9 alkyl substituted by substituent(s) independently selected from

••halogen,

••oxo,

••carbocyclic aryl,

••carbocyclic aryl substituted by methyl,

••carbocyclic aryloxy,

•C_1-C_7 alkoxy,

•halogenated C_1-C_7 alkoxy,

•C_1-C_7 alkoxy substituted by carbocyclic aryl,

•methylcarbonyloxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by methoxy,

•amino,

•di-methylamino,

•propargynylcarbonylamino substituted by carbocyclic aryl,

•carbocyclic arylsulfonylamino substituted by methyl,

•(carbocyclic aryl)NHC(O)NH substituted by halogenated methoxy,

•halogenated methylthio,

•carbocyclic arylthio substituted by cyano,

•di-propylamino sulfonyl,

•mono- or di- ethylaminocarbonyl substituted by carbocyclic aryl,

•carbocyclic aryl,

•heterocyclyl substituted by methyl,

•heterocyclyl substituted by halogenated carbocyclic aryl,

(vi) or heterocyclyl substituted by substituent(s) independently selected from

•halogen,

•nitro,

•C_1-C_4 alkyl,

•C_1-C_4 alkyl substituted by substituent(s) independently selected from

••halogen,

••methylthio substituted by halogenated carbocyclic aryl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

••heterocyclyl,

•methoxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by methyl,

•C_1-C_3 alkylthio,

•propenylthio,

•carbocyclic arylthio,

•C_1-C_3 alkylsulfonyl,

•carbocyclic arylsulfonyl,

•carbocyclic arylsulfonyl substituted by C_1-C_4 alkyl,

•carbocyclic aryl,

•halogenated carbocyclic aryl,

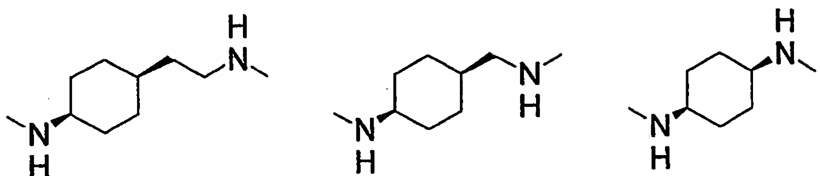
•carbocyclic aryl substituted by methyl,

•carbocyclic aryl substituted by nitro,

•heterocyclyl;

R_2 is methylamino or dimethylamino;

L is selected from Formula XX - XXII;



XX XXI XXII

Y is -C(O)-;

wherein carbocyclic aryl is phenyl, naphthyl, or biphenyl;

carbocyclyl is 1-oxo-indanyl, 9-oxo-fluorenyl, indenyl, anthraquinonyl, *C*-fluoren-9-ylidene, 1,2,3,4-tetrahydro-naphthyl, or bicyclo[2.2.1]hepteny;

heterocyclyl is 1,2,3-thiadiazolyl, 1,2,3-triazolyl, 1,2-dihydro-3-oxo-pyrazolyl, 1*H*-indolyl, 1*H*-pyrrolyl, 2,4-dihydro-3-oxo-pyrazolyl, 2*H*-benzopyranyl, 4-oxo-benzopyranyl, azetidinyl, benzo[b]thienyl, furyl, isoxazolyl, morpholinyl, piperidyl, piridyl, pyrazolyl, pyridyl, quinolyl, thiazolidyl, thiazolyl, thienyl, thiolanyl, 2,3-dihydro-1-oxo-isoindolyl, 2,3-dihydro-benzofuryl, 2-oxo-benzopyranyl, 2-oxo-pyrrolidinyl, 4-oxo-1,5,6,7-tetrahydro-indolyl, 9*H*-xanthenyl, cinnolyl, imidazolyl, morpholino, pyrimidyl, pyrrolidyl, tetrahydro-thienyl, benzofuranyl, or benzothiazolyl;

halogen is fluoro, chloro, bromo, or iodo.

Further other more preferred compounds of this invention are those compounds of Formula I wherein,

Q is Formula II;

R_1 represents

(i) C_1-C_5 alkyl substituted by substituent(s) independently selected from

•oxo,

•di-propylaminocarbonyl,

•methoxy substituted by carbocyclic aryl,

•methylcarbonyloxy,

•carbocyclic aryloxy,

•halogenated carbocyclic aryloxy,

•carbocyclic aryloxy substituted by nitro,

•heterocyclyloxy substituted by methyl,

•substituted heterocyclyl-ethylideneaminooxy,

•*tert*-butoxycarbonylamino,

•carbocyclic arylcarbonylamino,

•C_1-C_2 alkylthio,

•C_1-C_2 alkylthio substituted by substituent(s) independently selected from

••halogenated carbocyclic aryl,

••carbocyclic aryl substituted by methoxy,

•carbocyclic arylthio,

•hetrocyclylthio substituted by nitro,

•hetrocyclylthio substituted by methyl,

•cyclohexenyl,

•carbocyclyl substituted by substituent(s) independently selected from

••halogen,

••methyl,

••methoxy,

••ethenyl substituted by carbocyclic aryl substituted methylsulfinyl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••nitro,

•• C_1-C_4 alkyl,

••C_1-C_4 alkyl substituted by substituent(s) independently selected from

•••oxo,

•••carbocyclic aryl,

•••heterocyclyl,

••C_1-C_2 alkoxy,

••halogenated C_1-C_2 alkoxy,

••C_1-C_2 alkoxy substituted by carbocyclic aryl,

••carbocyclic aryloxy,

••halogenated mono-carbocyclic arylaminocarbonyl,

••carbocyclic aryl,

••heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••C_1-C_2 alkyl,

•• C_1-C_2 substituted by carbocyclic aryl,

••methoxy,

••methoxy substituted by carbocyclic aryl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

(ii) C_2-C_3 alkenyl substituted by substituent(s) independently selected from

•carbocyclic aryl,

•halogenated carbocyclic aryl,

•carbocyclic aryl substituted by nitro,

(iii) C_3-C_6 cycloalkyl substituted by substituent(s) independently selected from

•methyl substituted by oxo,

•methyl substituted by carbocyclic aryl,

•carbocyclic aryl,

(iv) carbocyclyl,

(v) carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•cyano,

•nitro,

•C_1-C_4 alkyl,

•C_1-C_2 alkyl substituted by substituent(s) independently selected from

••halogen,

••oxo,

••carbocyclic aryl,

••carbocyclic aryl substituted by methyl,

••carbocyclic aryloxy,

•C_1-C_2 alkoxy,

•halogenated C_1-C_2 alkoxy,

•C_1-C_2 alkoxy substituted by carbocyclic aryl,

•methylcarbonyloxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by methoxy,

•amino,

•di-methylamino,

•propargynylcarbonylamino substituted by carbocyclic aryl,

•carbocyclic arylsulfonylamino substituted by methyl,

•(carbocyclic aryl)NHC(O)NH substituted by halogenated methoxy,

•halogenated methylthio,

•carbocyclic arylthio substituted by cyano,

•di-propylamino sulfonyl,

•mono- or di- ethylaminocarbonyl substituted by carbocyclic aryl,

•carbocyclic aryl,

•heterocyclyl substituted by methyl,

•heterocyclyl substituted by halogenated carbocyclic aryl,

(vi) or heterocyclyl substituted by substituent(s) independently selected from

•halogen,

•nitro,

•C_1-C_4 alkyl,

•C_1-C_4 alkyl substituted by substituent(s) independently selected from

••halogen,

••methylthio substituted by halogenated carbocyclic aryl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

••heterocyclyl,

•methoxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by methyl,

•C_1-C_3 alkylthio,

•propenylthio,

•carbocyclic arylthio,

•C_1-C_3 alkylsulfonyl,

•carbocyclic arylsulfonyl,

•carbocyclic arylsulfonyl substituted by methyl,

•carbocyclic aryl,

•halogenated carbocyclic aryl,

•carbocyclic aryl substituted by methyl,

•carbocyclic aryl substituted by nitro,

•heterocyclyl;

R_2 is methylamino or dimethylamino;

L is selected from Formula XX - XXII;

Y is -C(O)-;

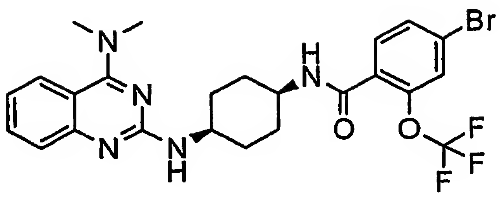
wherein carbocyclic aryl is phenyl , naphthyl, or biphenyl;

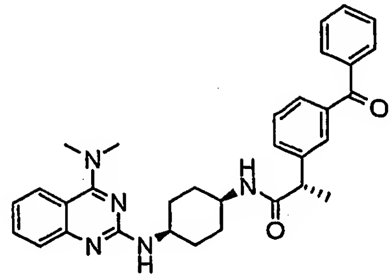
carbocyclyl is 1-oxo-indanyl, indenyl, 9-oxo-fluorenyl, 1,2,3,4-tetrahydro-naphthyl, or bicyclo[2.2.1]hepteny;

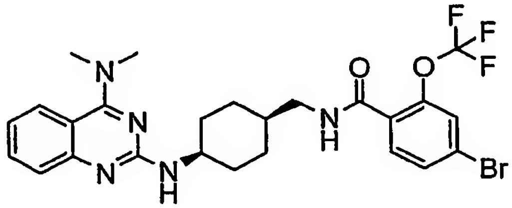
heterocyclyl is 1*H*-indolyl, 2,4-dihydro-3-oxo-pyrazolyl, furyl, pyrazolyl, pyridyl, thienyl, 1,2,3-triazolyl, 1*H*-pyrrolyl, 2,3-dihydro-1-oxo-isoindolyl, 2,3-dihydro-benzofuryl, 2*H*-benzopyranyl, 2-oxo-benzopyranyl, 4-oxo-1,5,6,7-tetrahydro-indolyl, imidazolyl, isoxazolyl, morpholino, morpholinyl, pyrazolyl, pyrimidyl, quinolyl, thiazolyl, tetrahydro-thienyl, benzofuranyl, or benzothiazolyl;

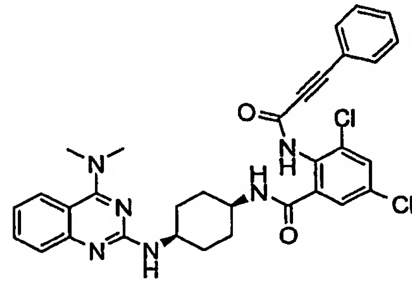
halogen is fluoro, chloro, bromo, or iodo.

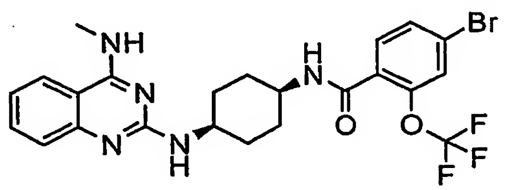
The following compounds are specially preffered;

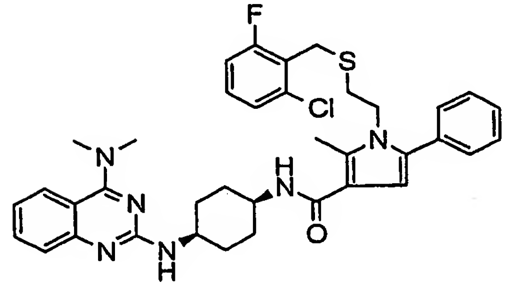
 ,

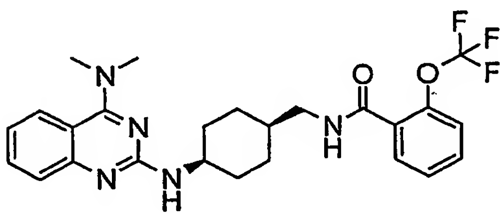
 ,

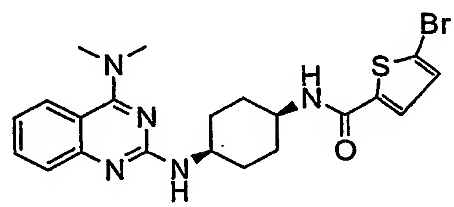
 ,

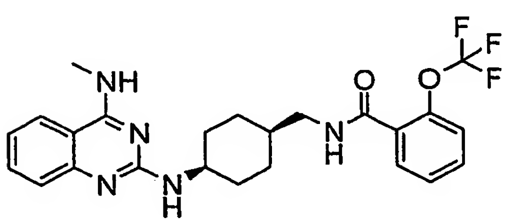
 ,

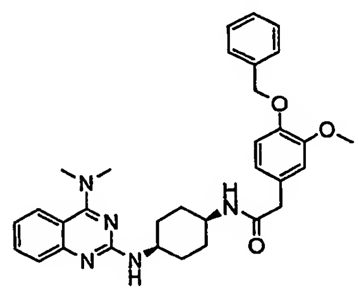
 ,

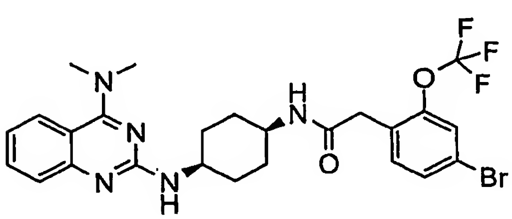
 ,

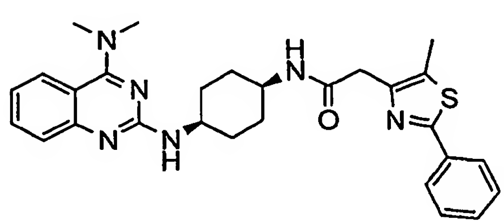
 ,

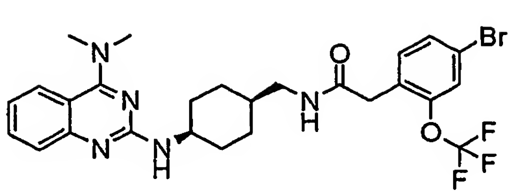
 ,

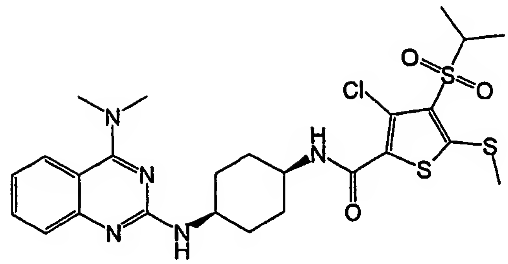
 ,

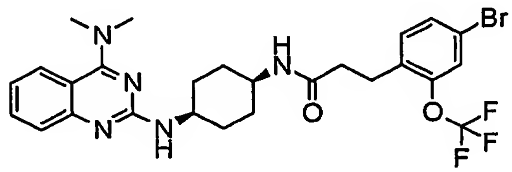
 ,

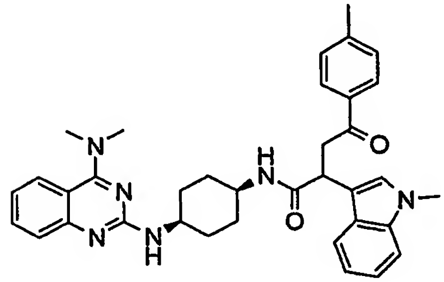
 ,

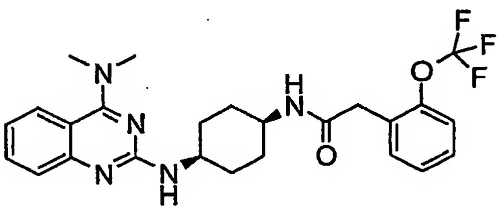
 ,

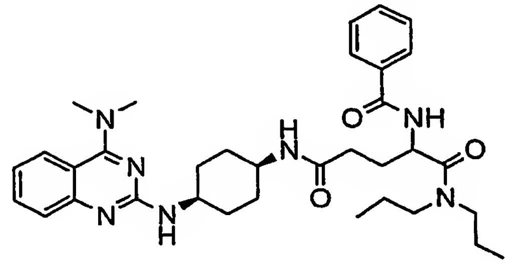
 ,

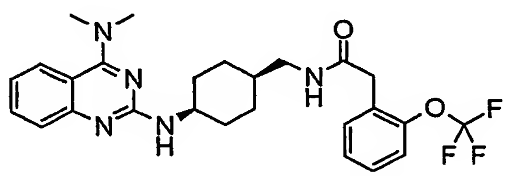
 ,

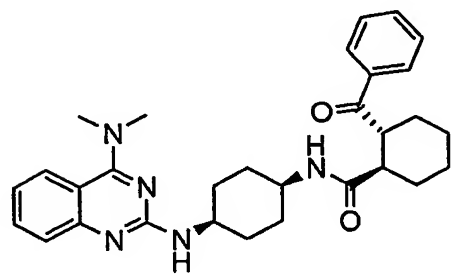
 ,

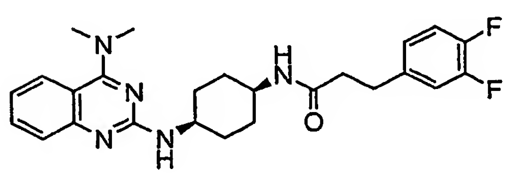
 ,

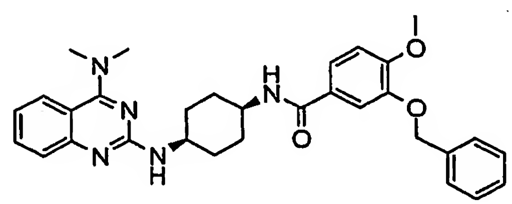
 ,

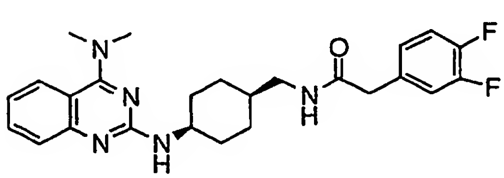
 ,

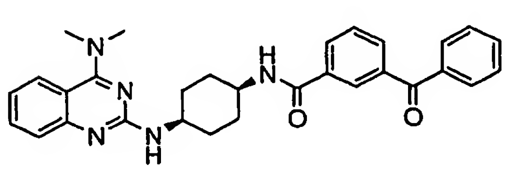
 ,

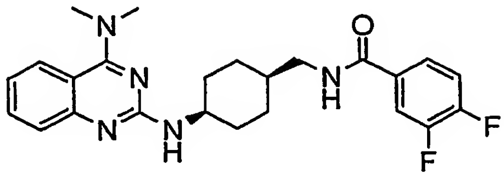
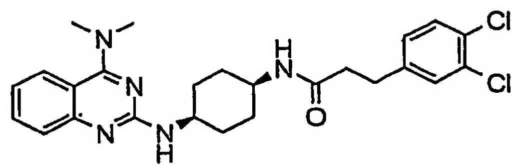
 ,

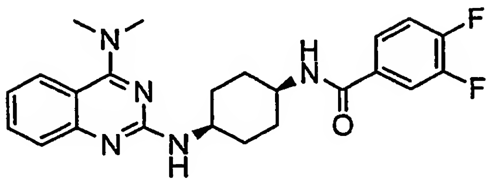
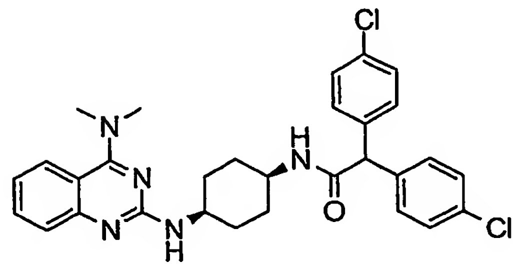
 ,

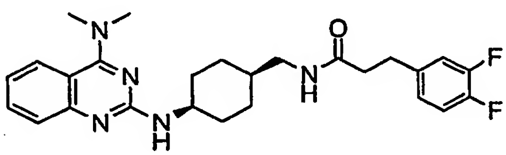
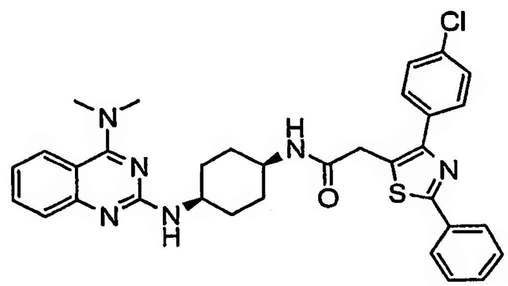
 ,

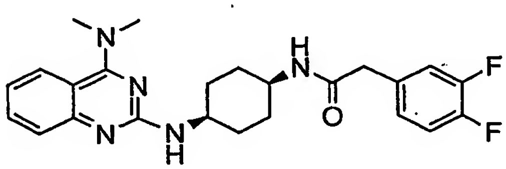
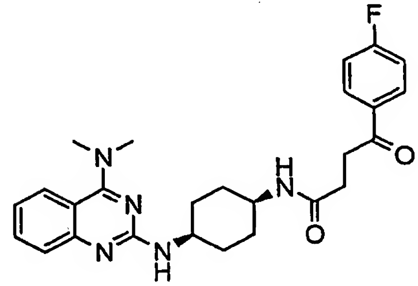
 ,

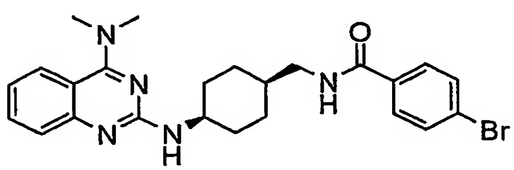
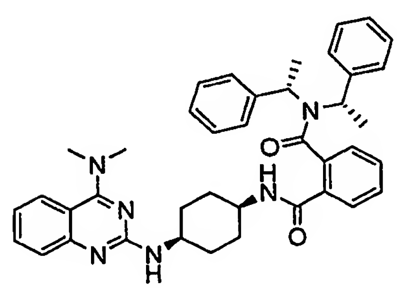
 ,

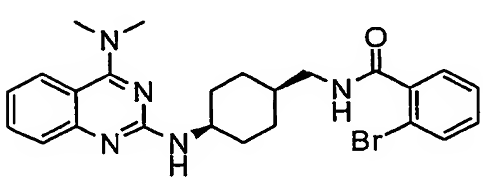
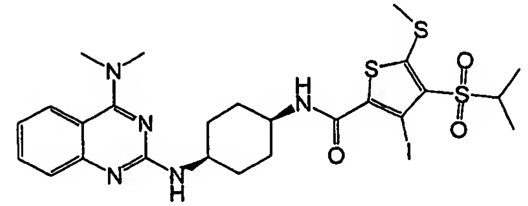
 ,  ,

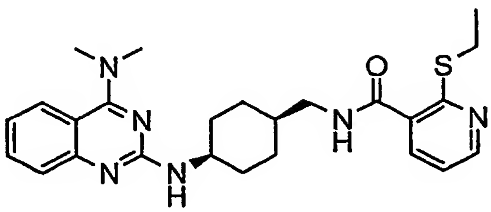
 ,  ,

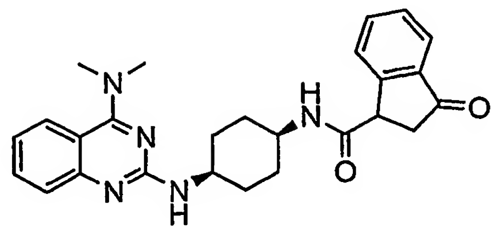
 ,  ,

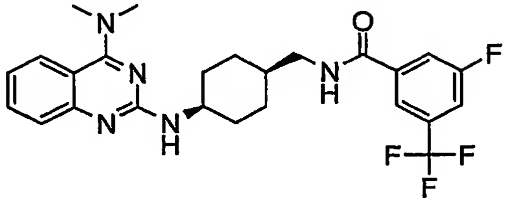
 ,  ,

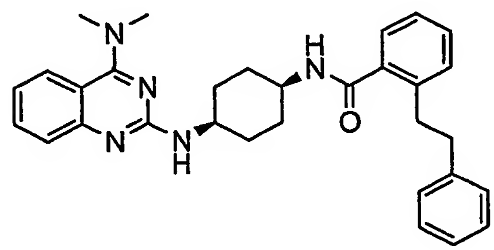
 ,  ,

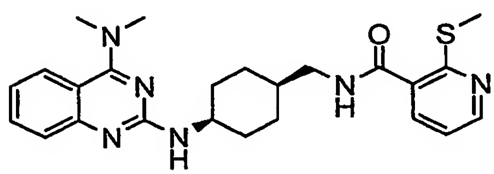
 ,  ,

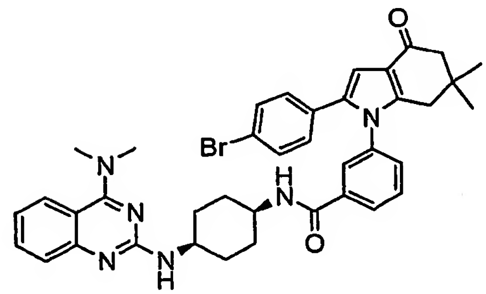
 ,

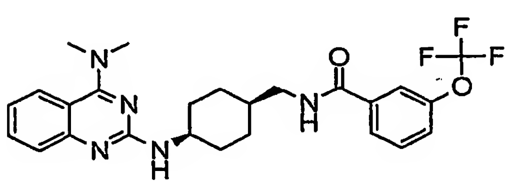
 ,

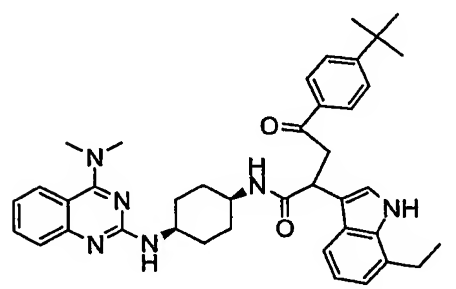
 ,

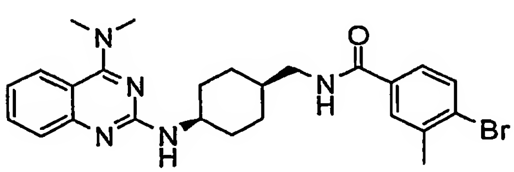
 ,

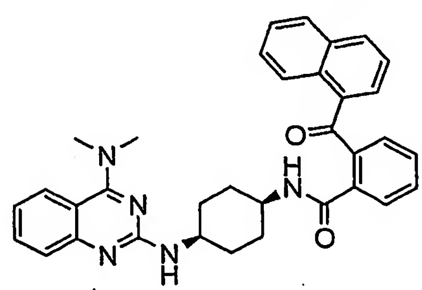
 ,

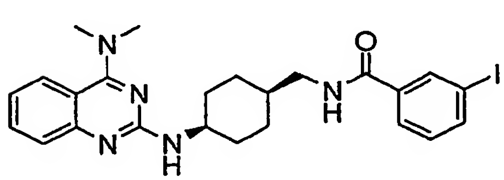
 ,

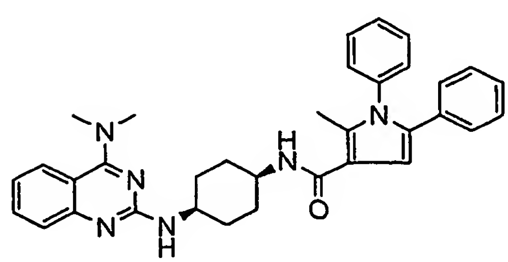
 ,

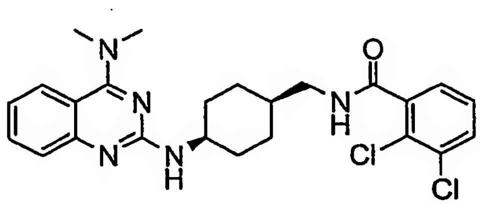
 ,

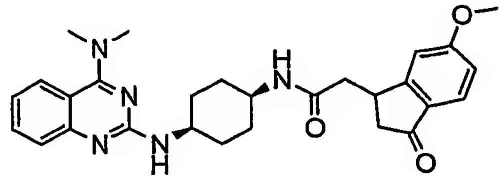
 ,

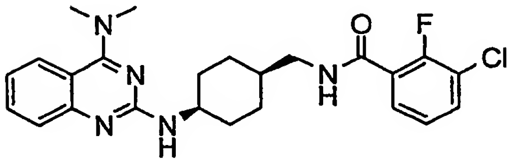
 ,

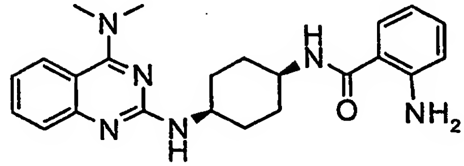
 ,

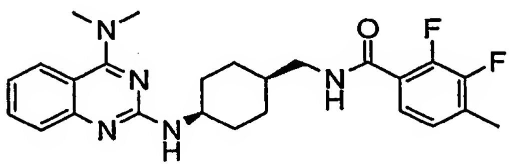
 ,

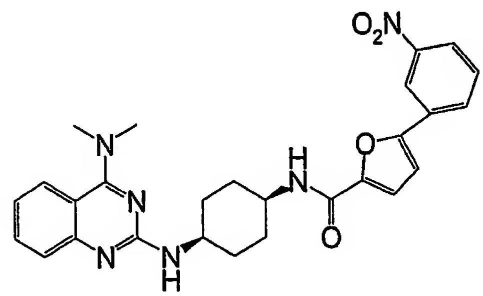
 ,

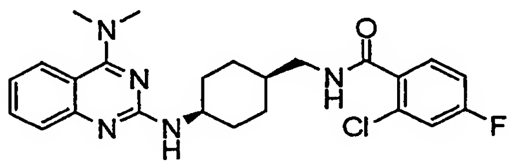
 ,

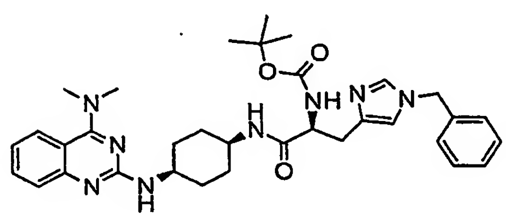
 ,

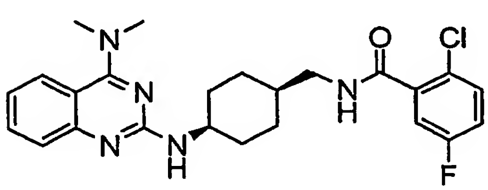
 ,

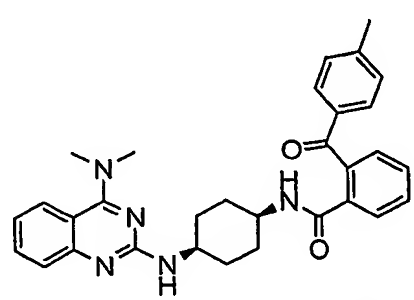
 ,

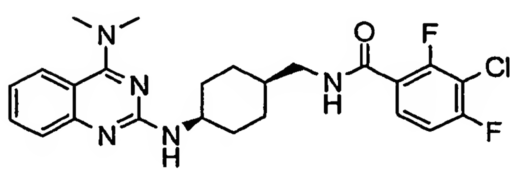
 ,

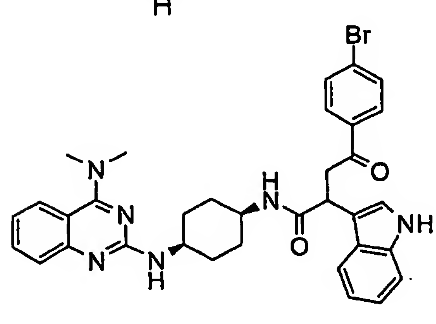
 ,

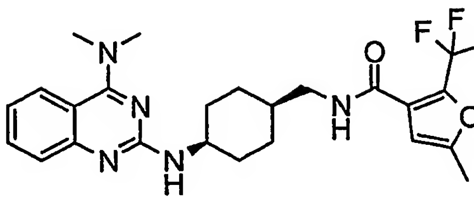
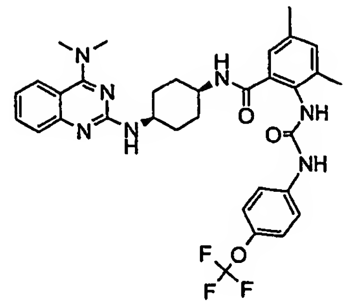
 ,

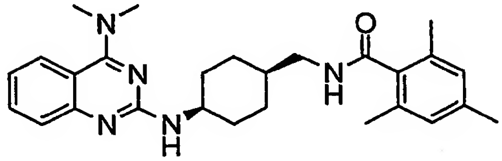
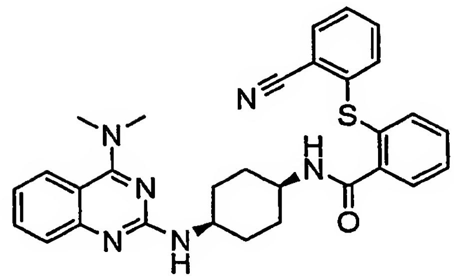
 ,

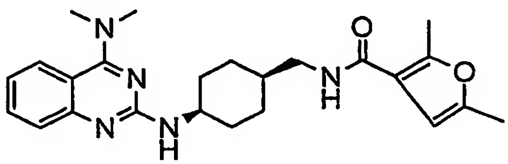
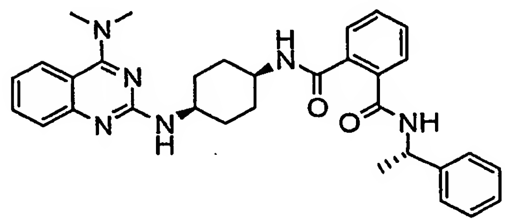
 ,

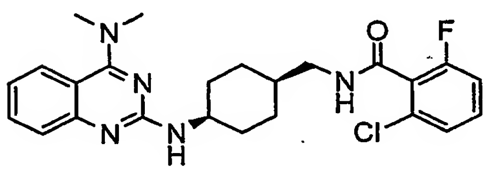
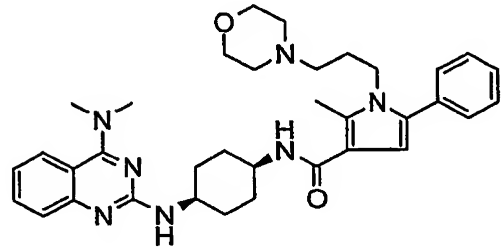
 ,

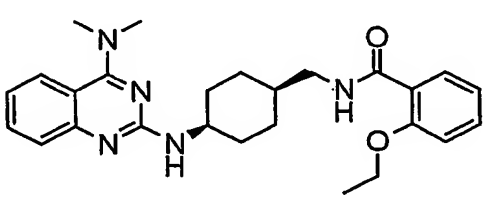
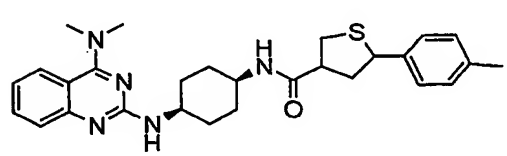
 ,

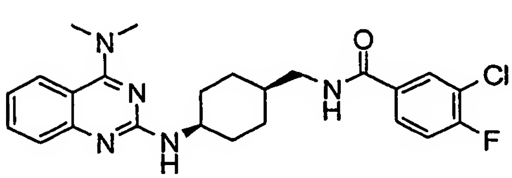
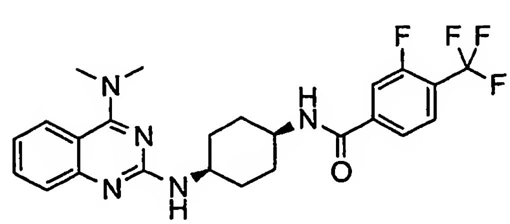
 ,  ,

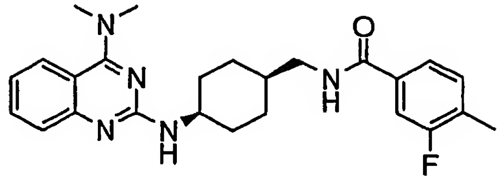
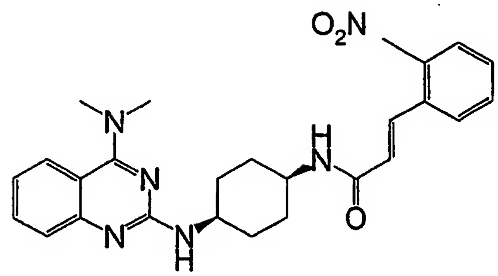
 ,  ,

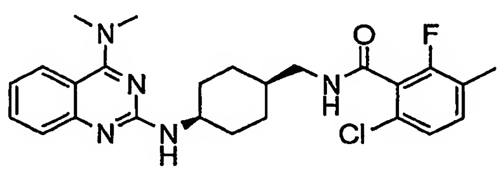
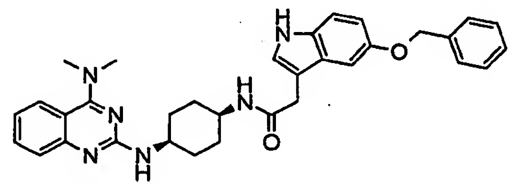
 ,  ,

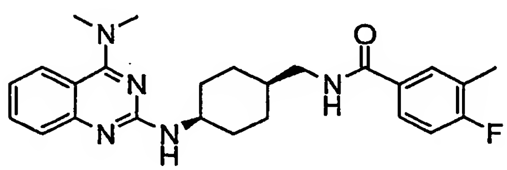
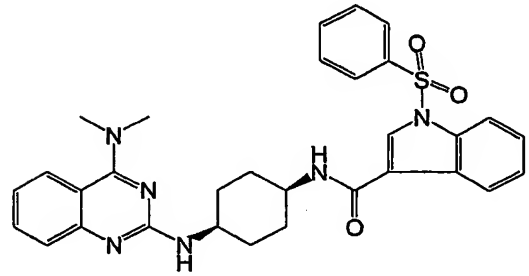
 ,  ,

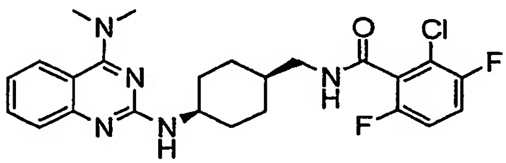
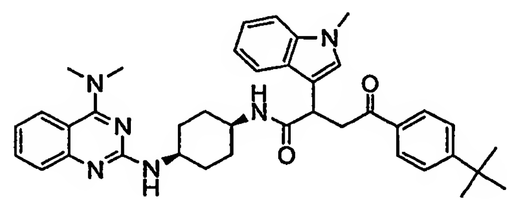
 ,  ,

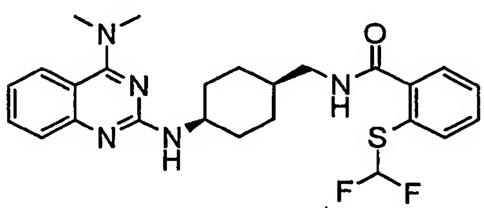
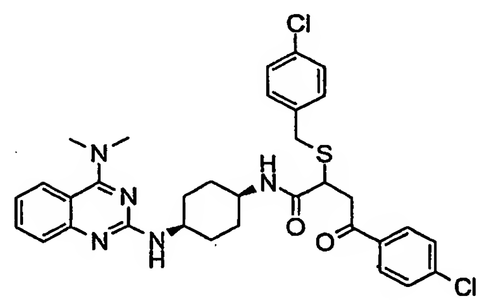
 ,  ,

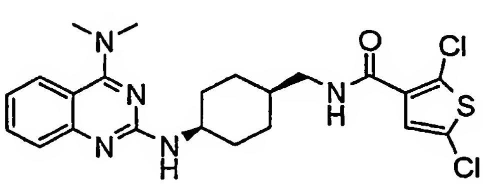
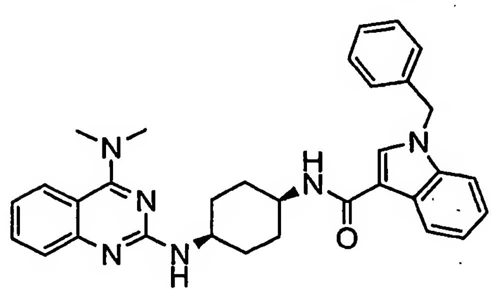
 ,  ,

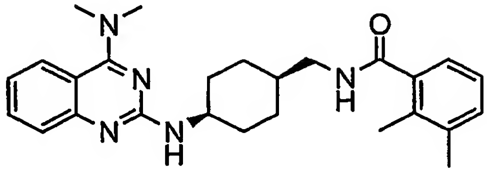
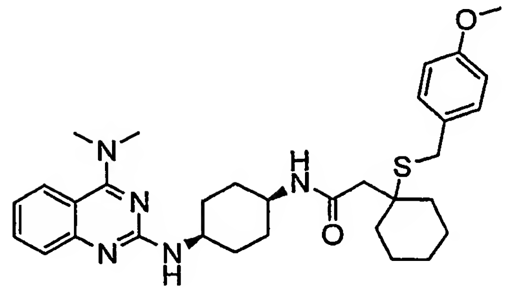
 ,  ,

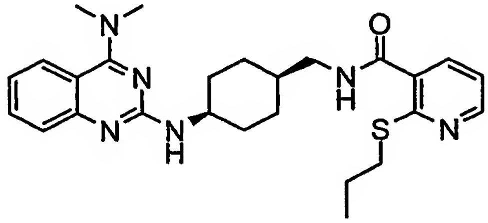
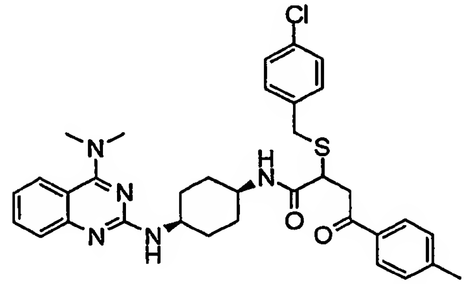
 ,  ,

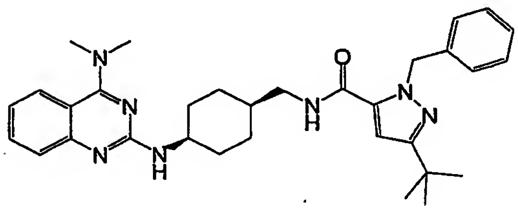
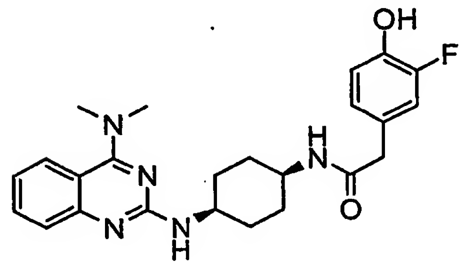
 ,  ,

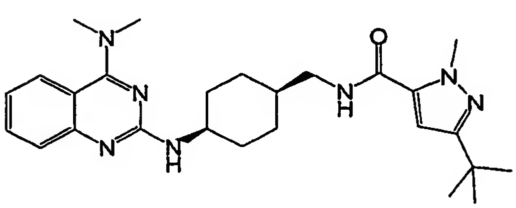
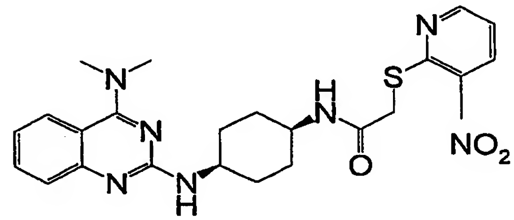
 ,  .

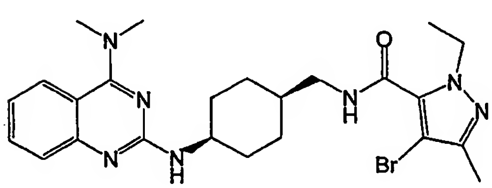
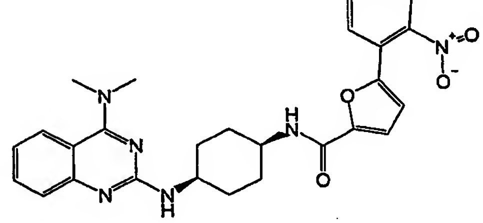
 ,  ,

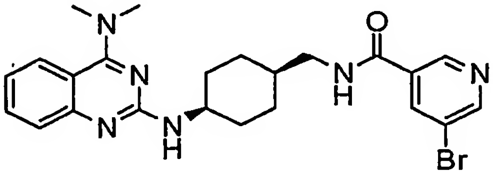
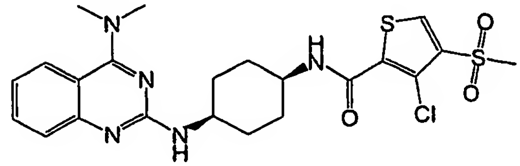
 ,  ,

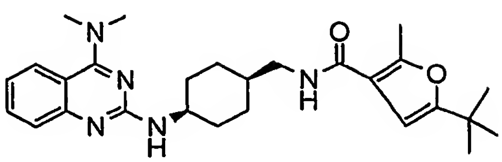
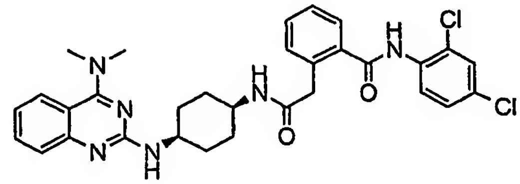
 ,  ,

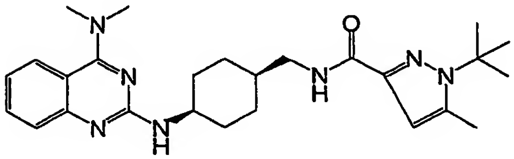
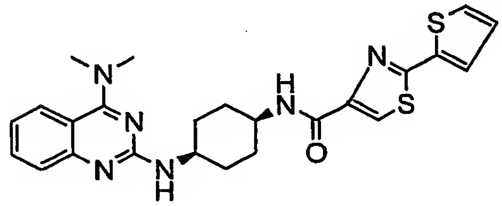
 ,  ,

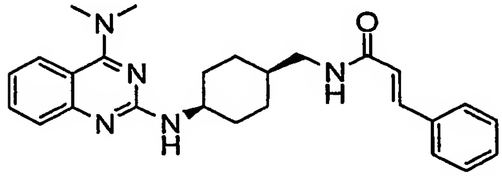
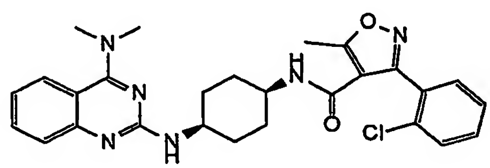
 ,  ,

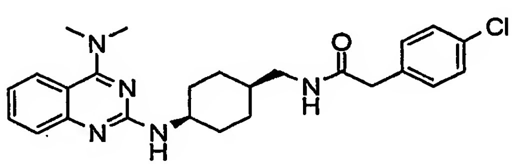
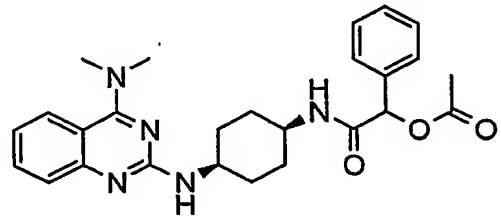
 ,  ,

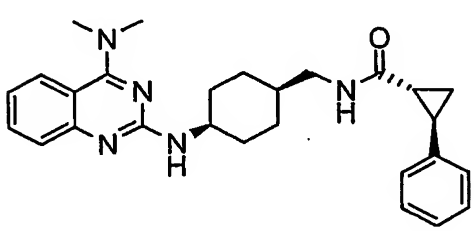
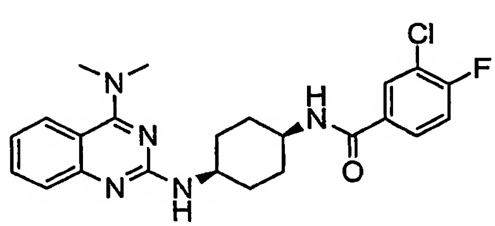
 ,  ,

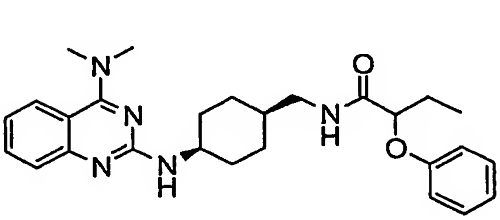
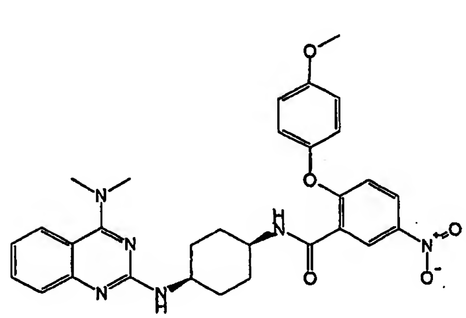

,

,

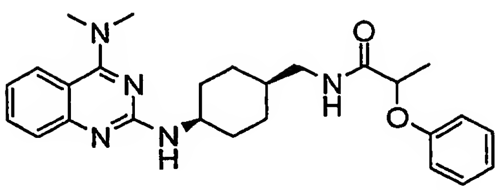
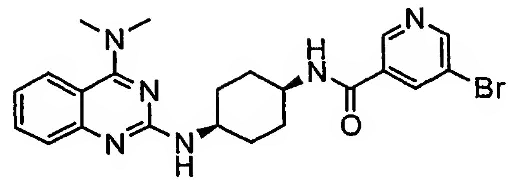

,

,

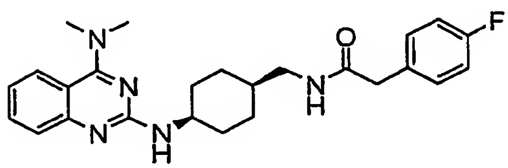
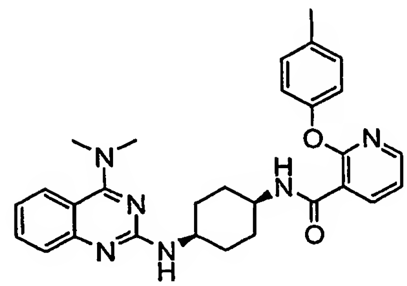

,

,

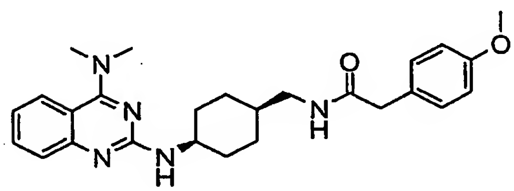
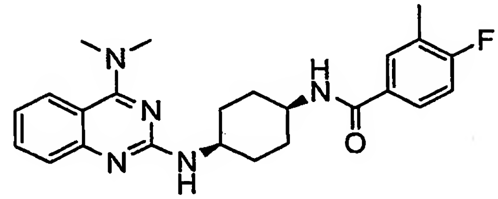

,

,

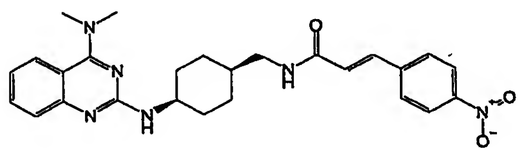
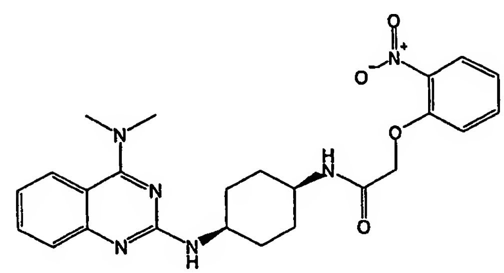

,

,

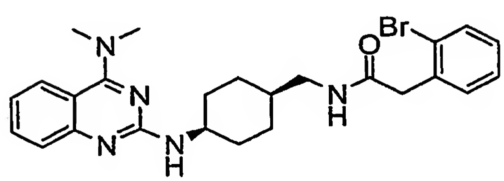
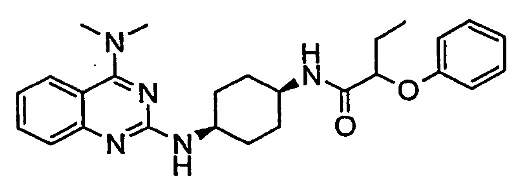

,

,

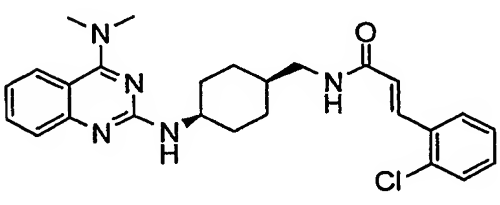
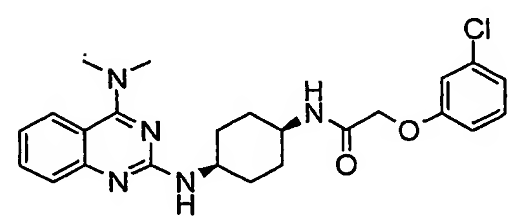
 ,  ,

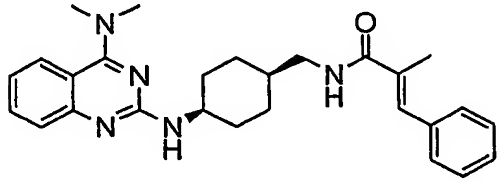
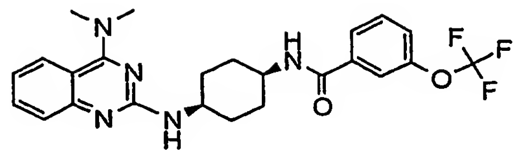
 ,  ,

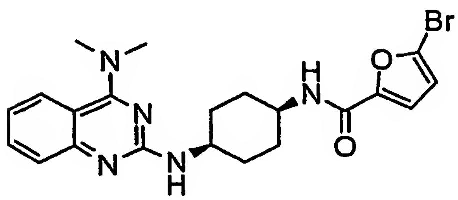
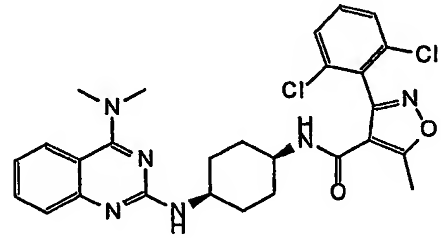
 ,  ,

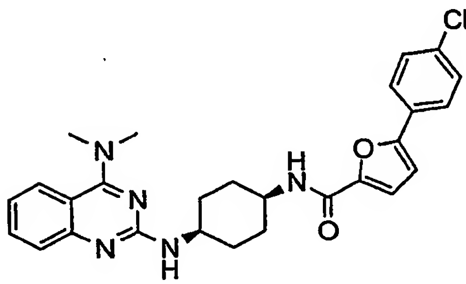
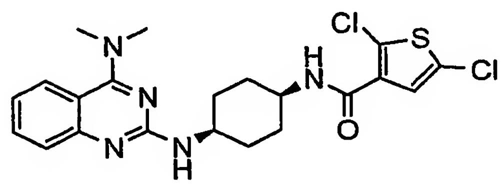
 ,  ,

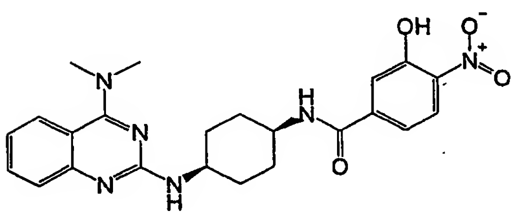
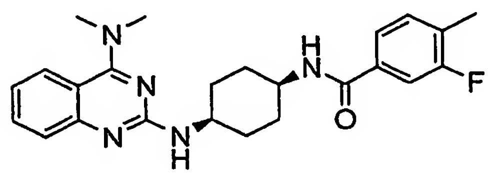
 ,  ,

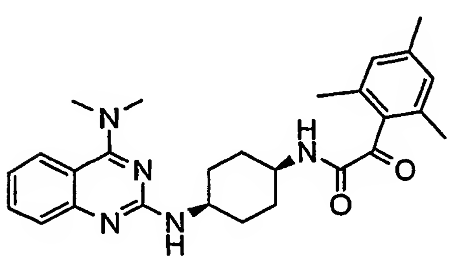
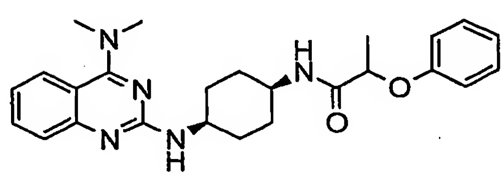
 ,  ,

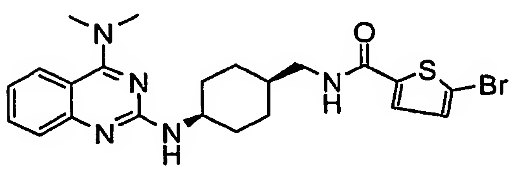
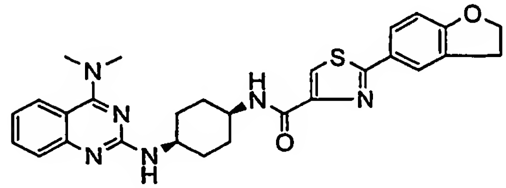
 ,  ,

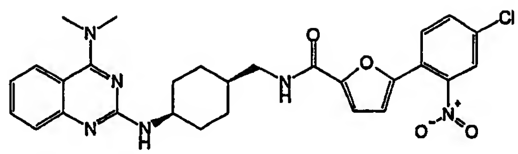
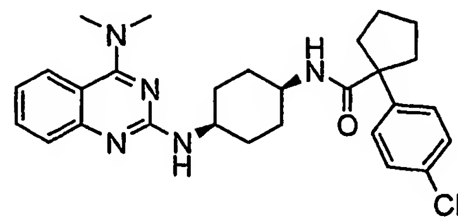
 ,  ,

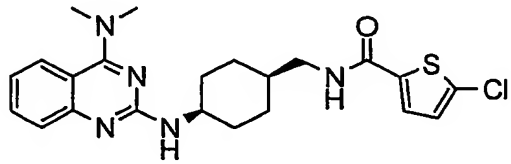
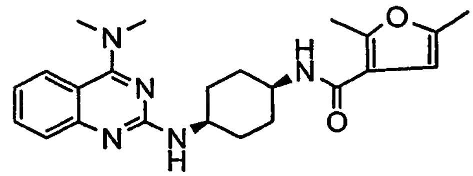
 ,  ,

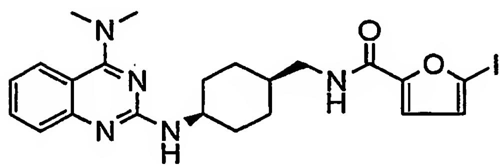
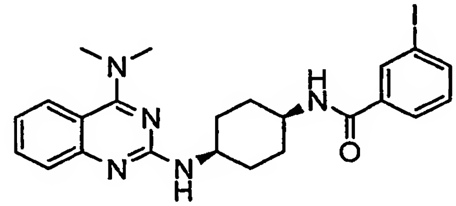
 ,  ,

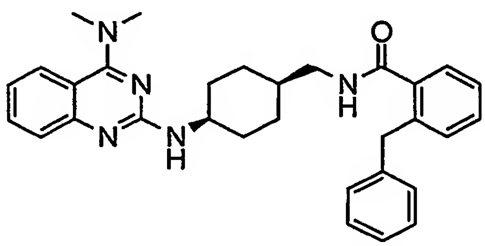
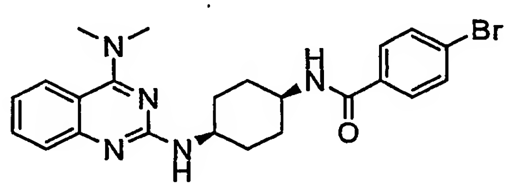
 ,  ,

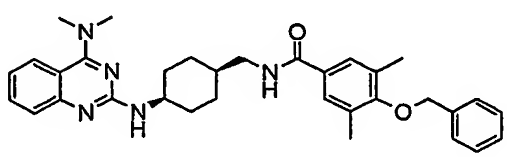
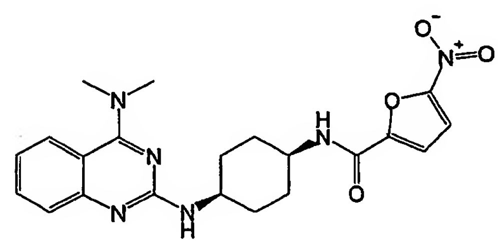
 ,  ,

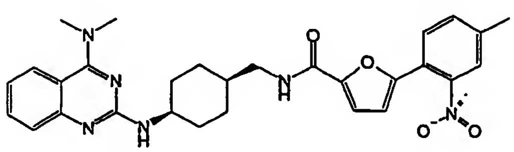
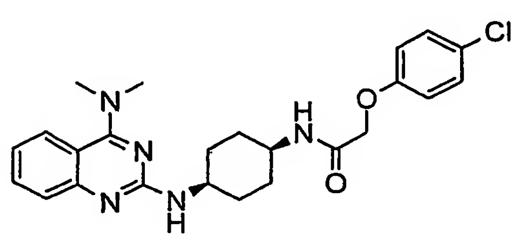

,

,

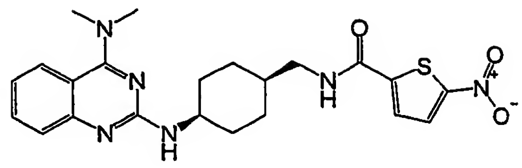
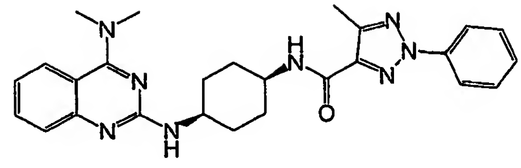
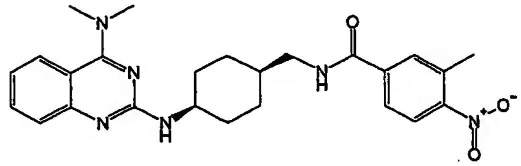
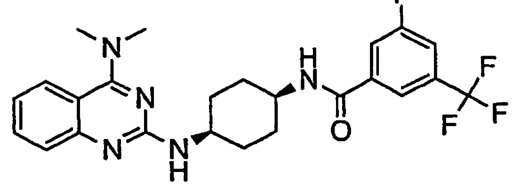
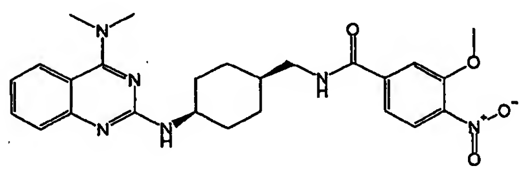
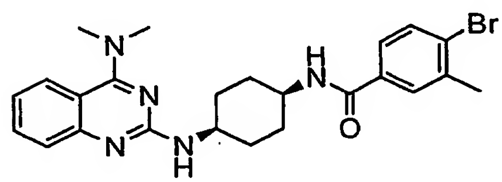
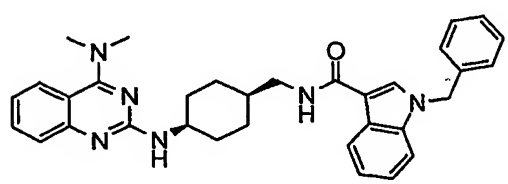
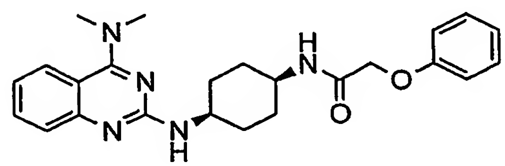
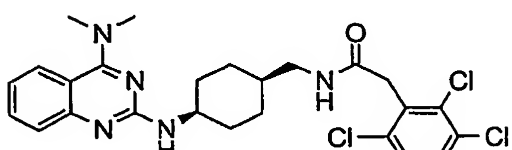
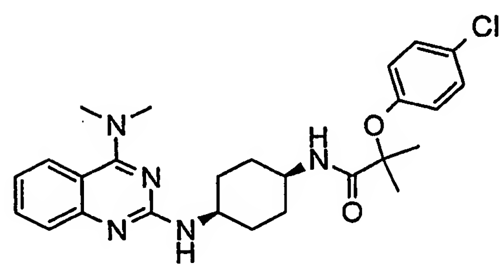
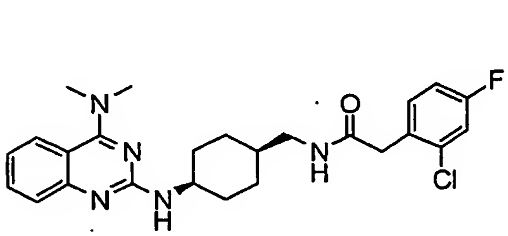
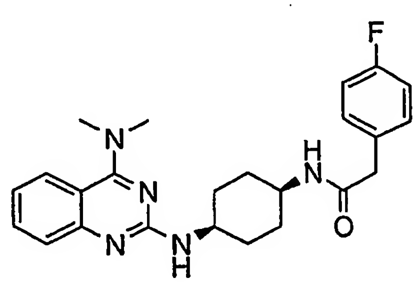

,

,

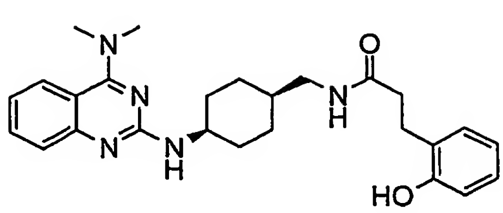

,

,

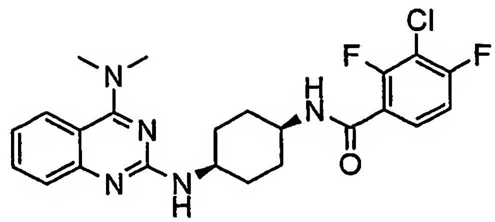

,

,

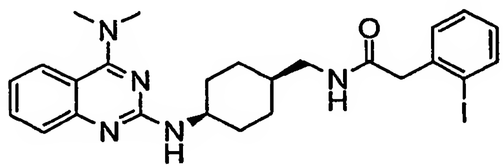

,

,

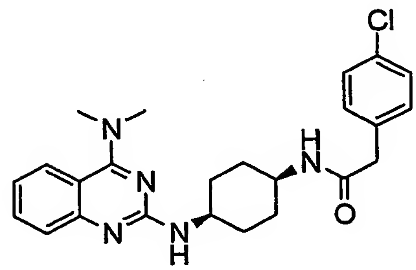

,

,

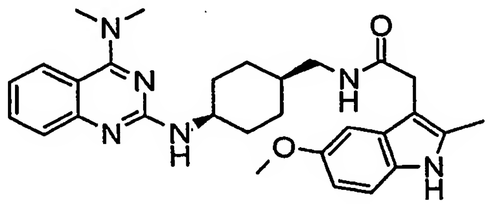

,

,

,

,

,

,

,

,

,

,

,

,

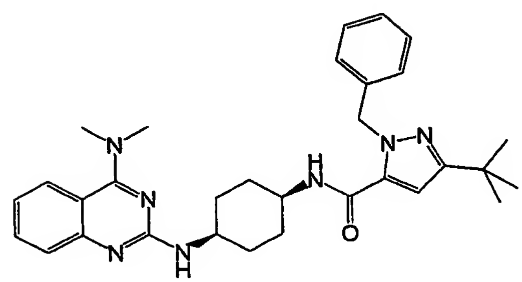
 ,

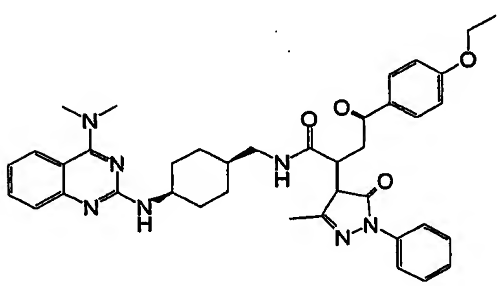
 ,

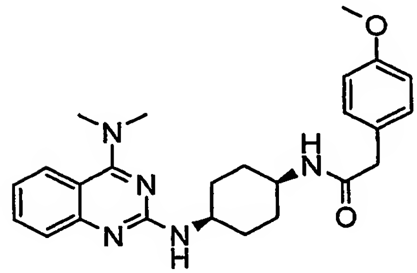
 ,

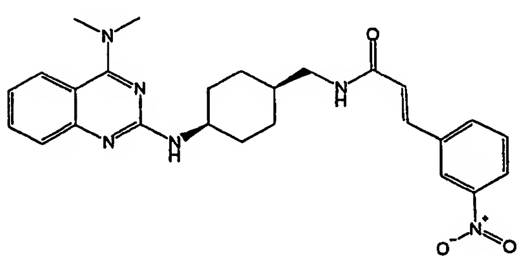
 ,

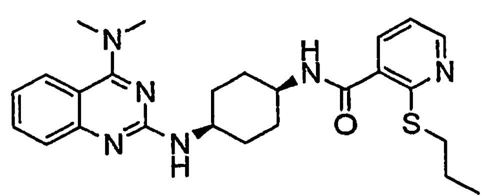
 ,

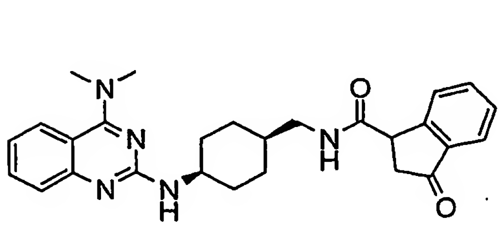
 ,

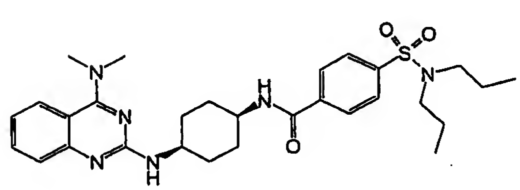
 ,

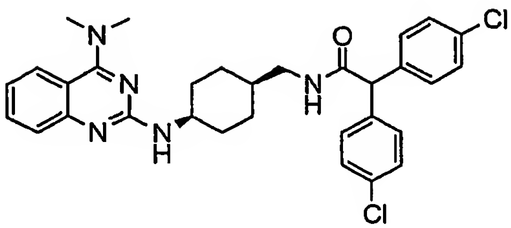
 ,

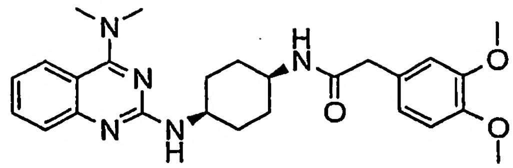
 ,

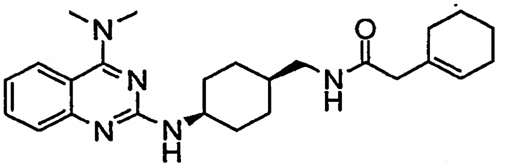
 ,

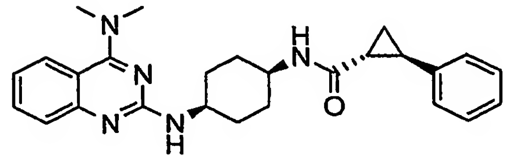
 ,

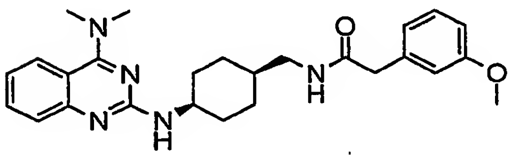
 ,

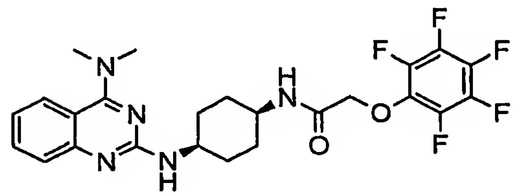
 ,

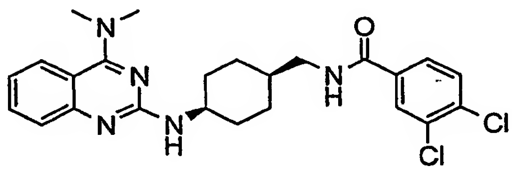
 ,

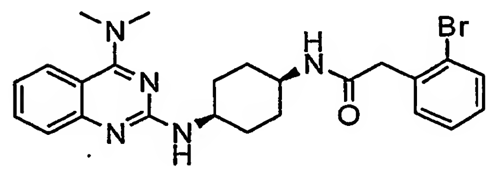
 ,

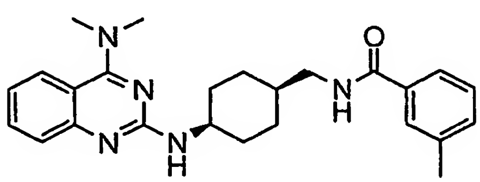
 ,

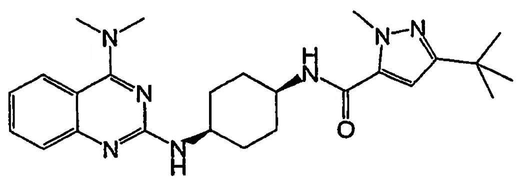
 ,

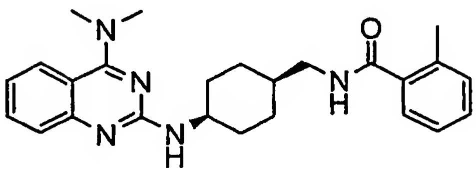
 ,

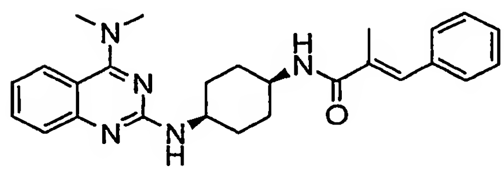
 ,

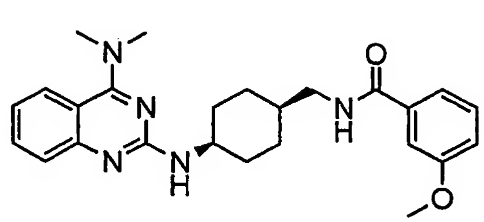
 ,

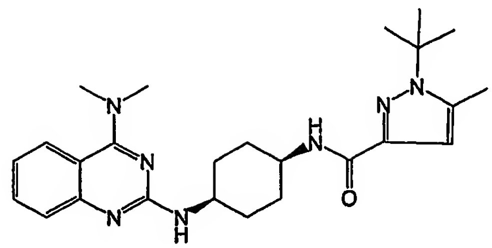
 ,

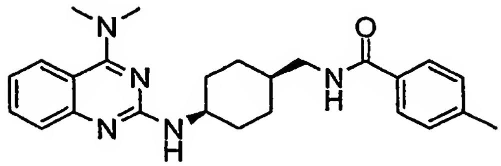
 ,

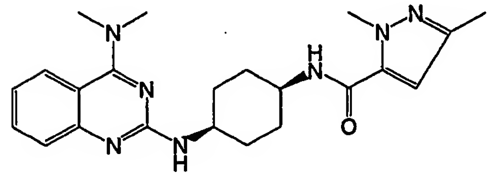
 ,

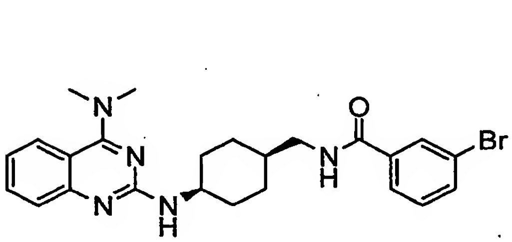
 ,

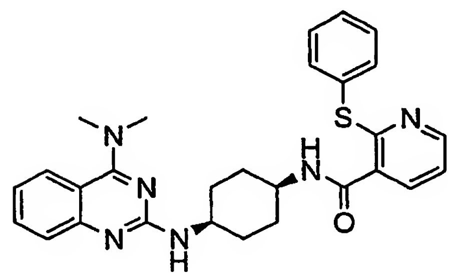
 ,

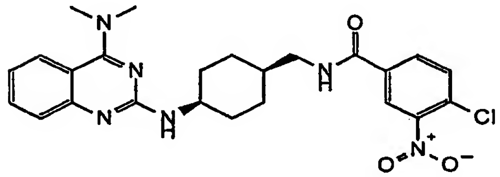
 ,

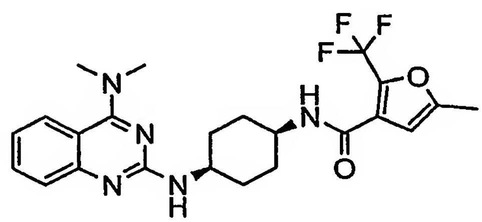
 ,

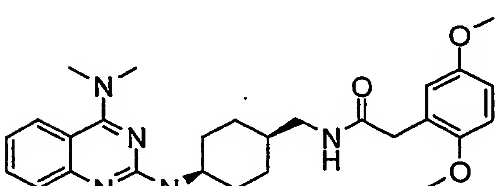
 ,

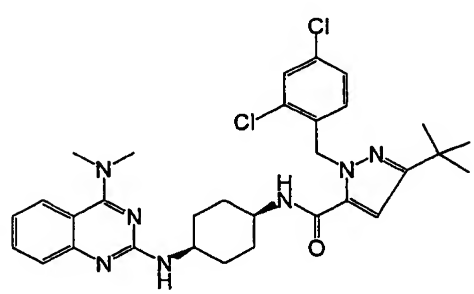
 ,

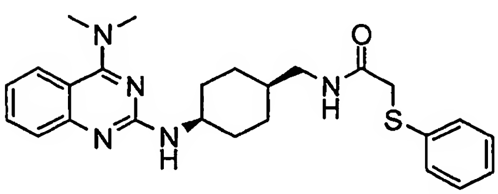
 ,

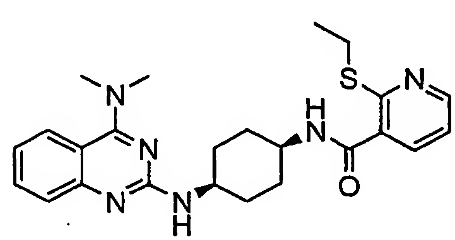
 ,

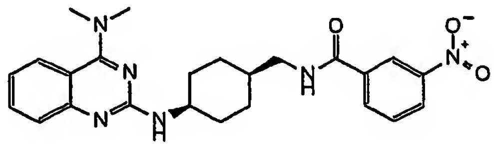
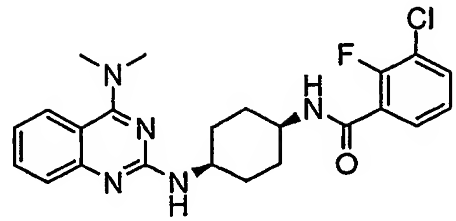
 ,

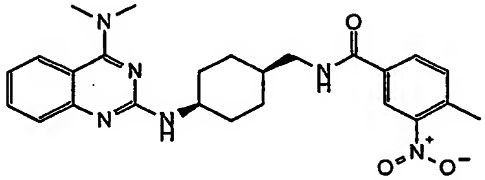
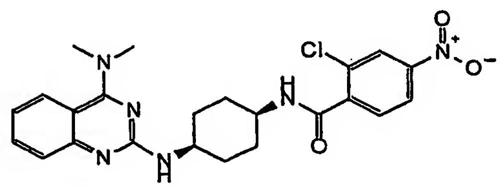
 ,

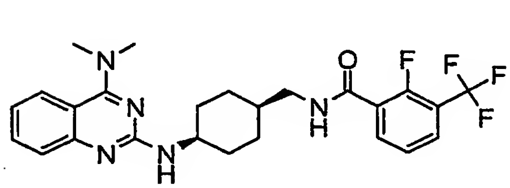
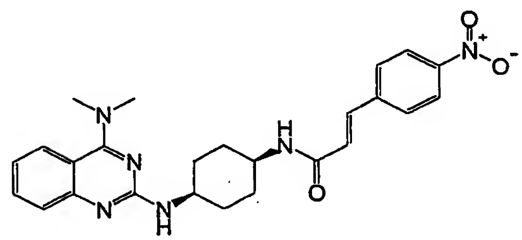
 ,

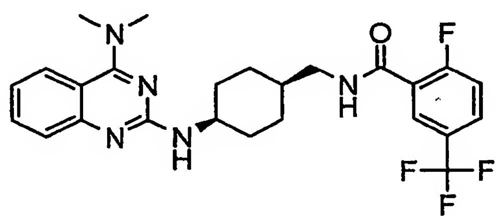
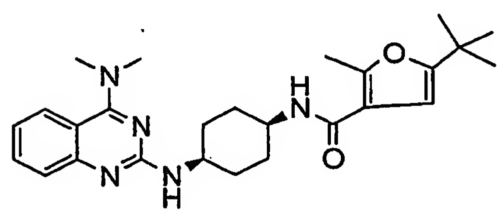
 ,

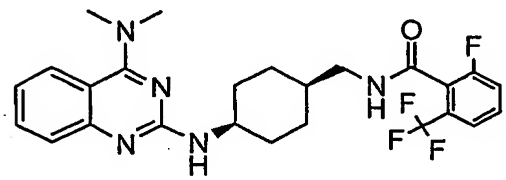
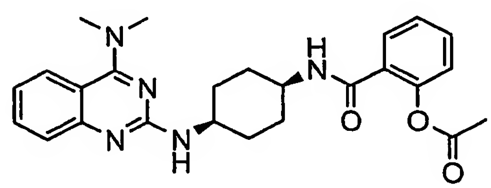
 ,

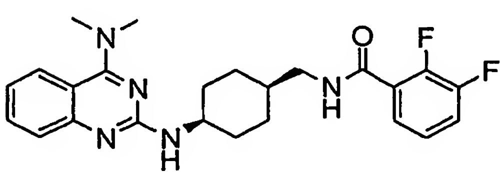
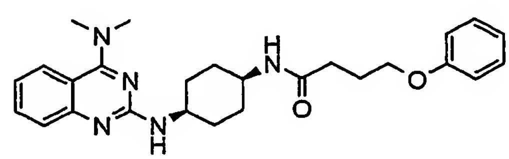

,

,

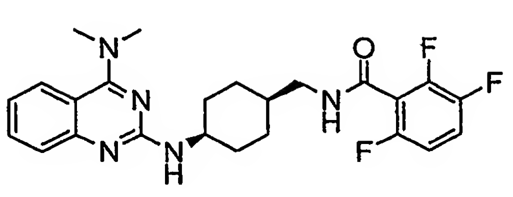
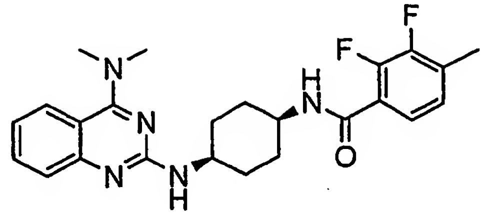
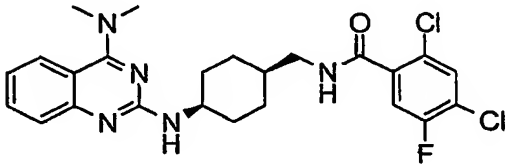
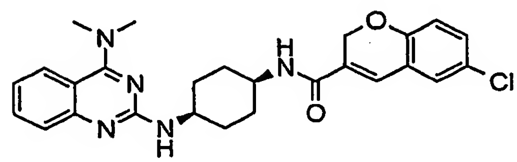
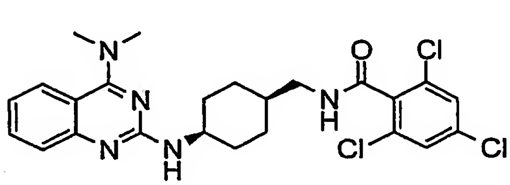
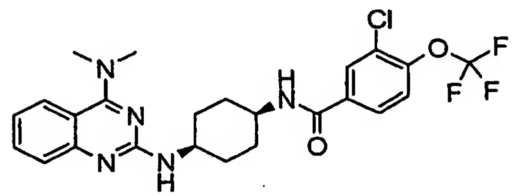
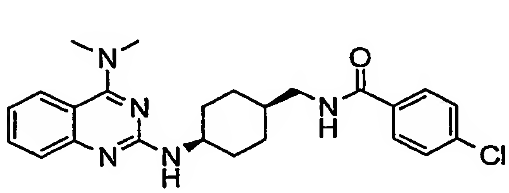
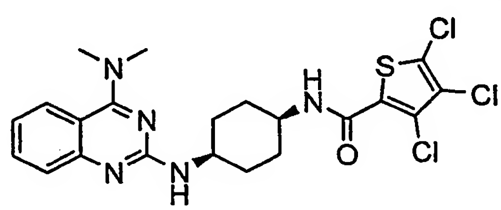
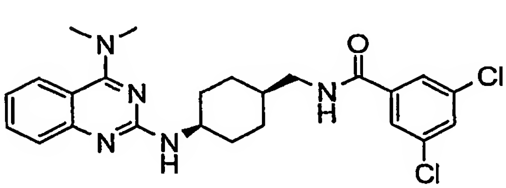
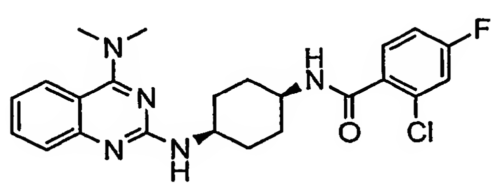
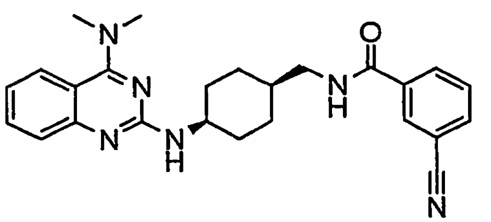
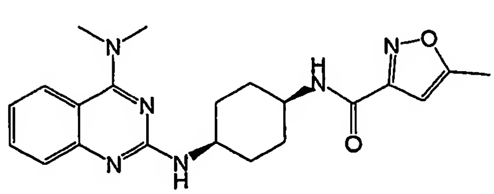

,

,

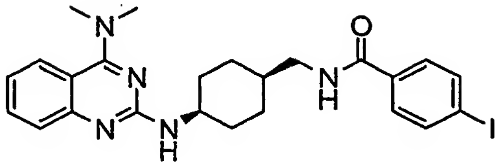

,

,

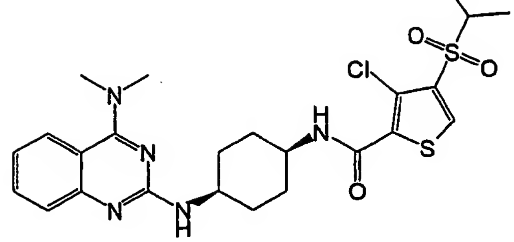

,

,

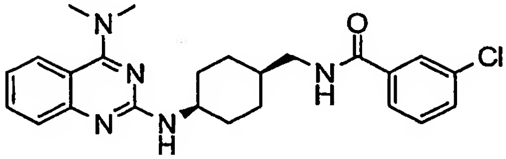

,

,

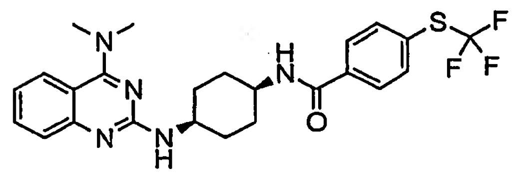

,

,

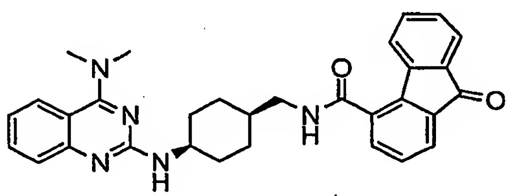

,

,

,

,

,

,

,

,

,

,

,

,

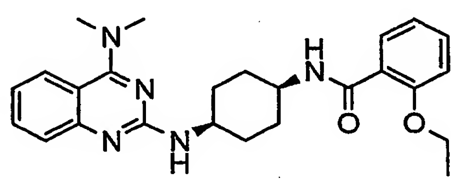
 ,

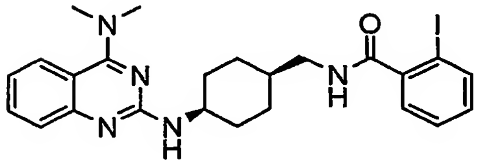
 ,

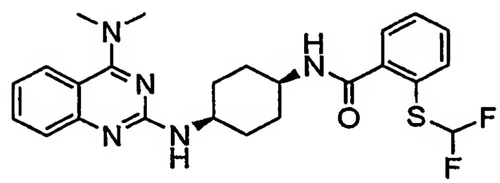
 ,

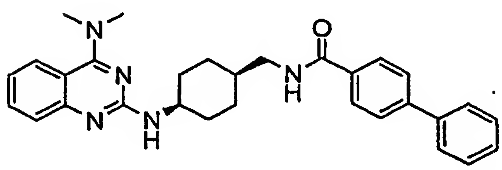
 ,

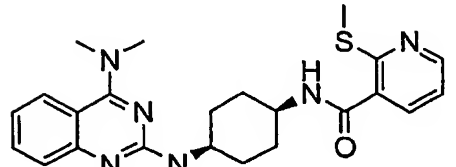
 ,

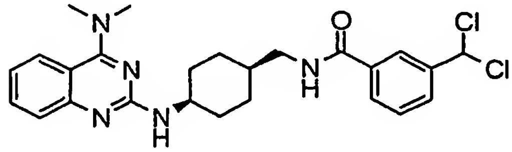
 ,

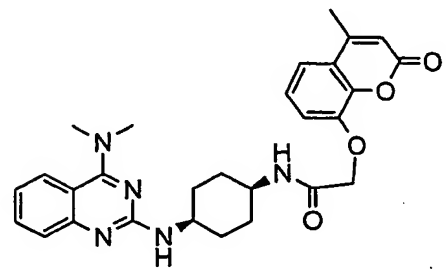
 ,

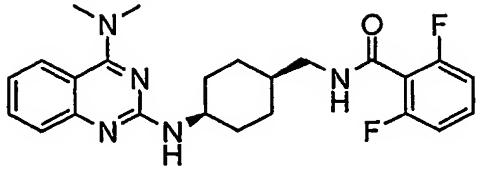
 ,

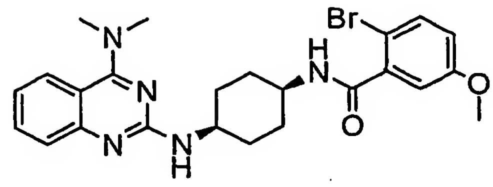
 ,

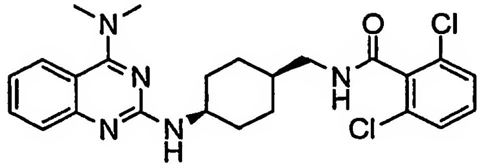
 ,

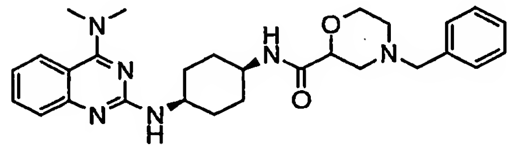
 ,

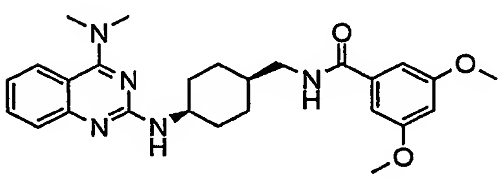
 ,

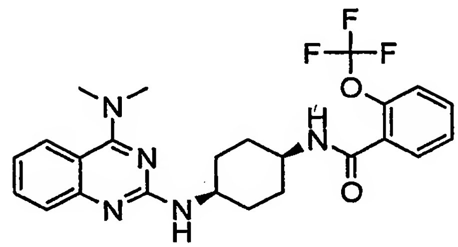
 ,

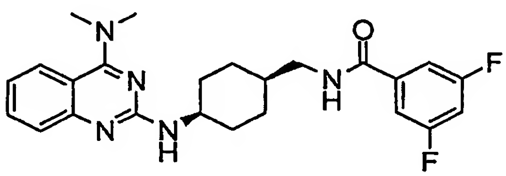
 ,

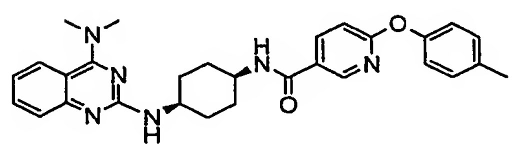
 ,

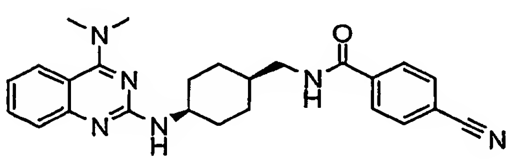
 ,

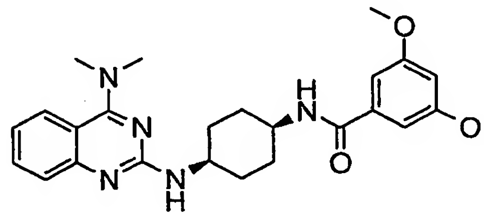
 ,

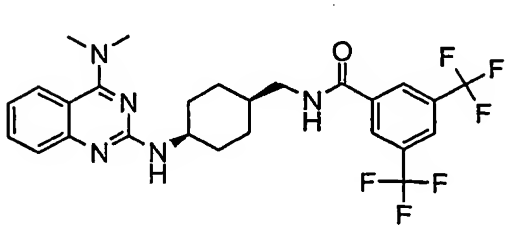
 ,

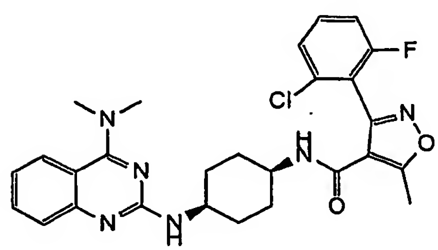
 ,

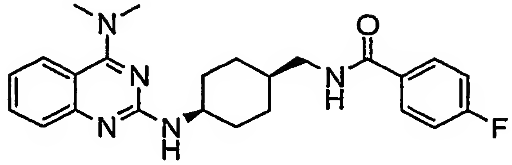
 ,

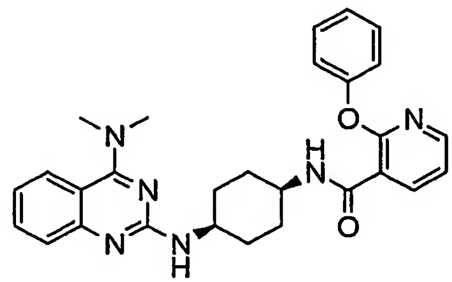
 ,

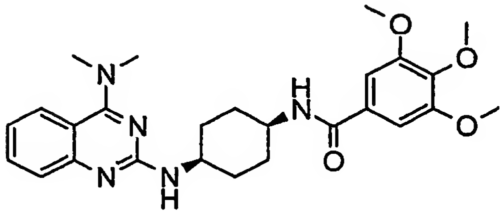
 ,

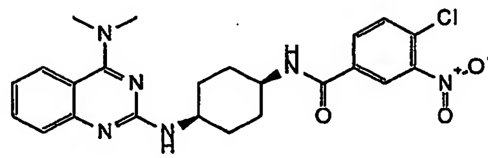
 ,

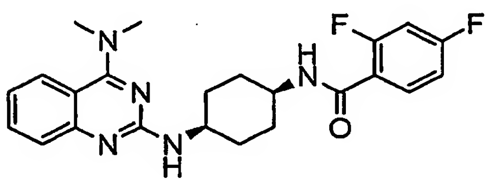
 ,

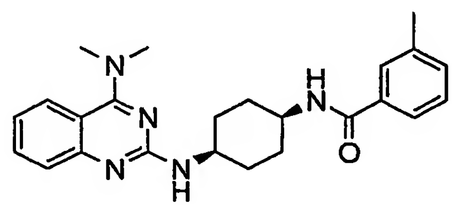
 ,

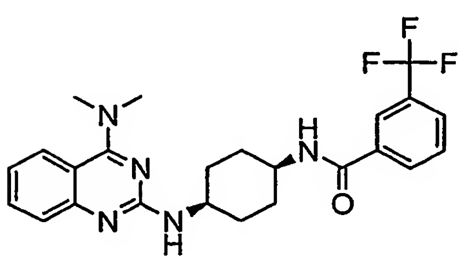
 ,

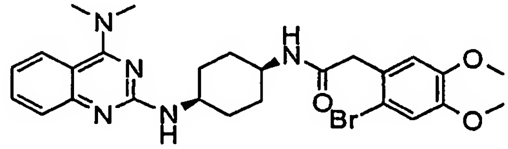
 ,

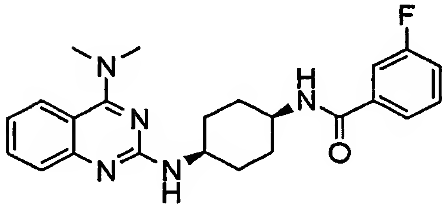
 ,

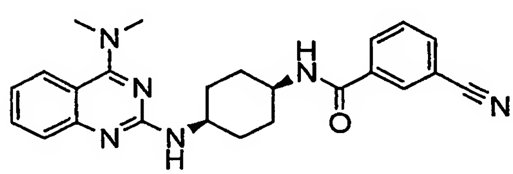
 ,

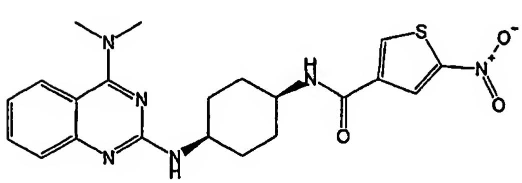
 ,

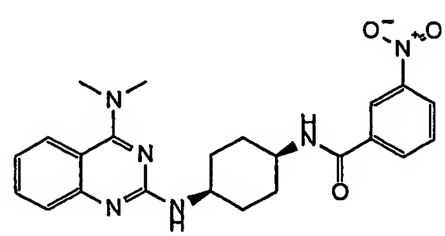
 ,

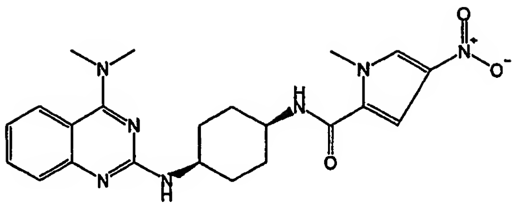
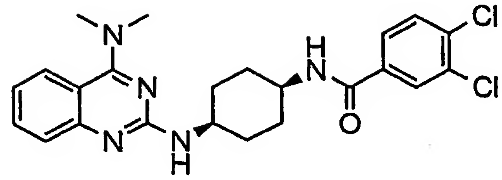
 ,

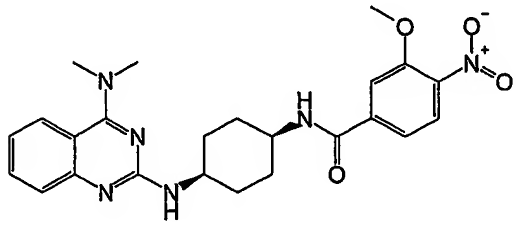
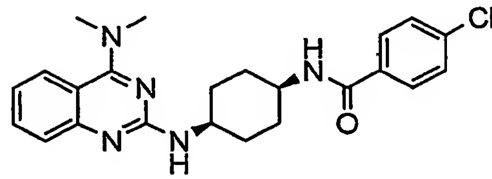
 ,

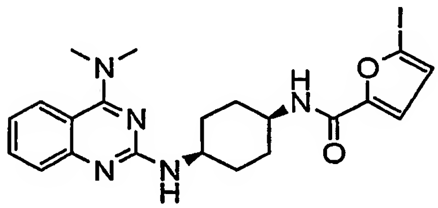
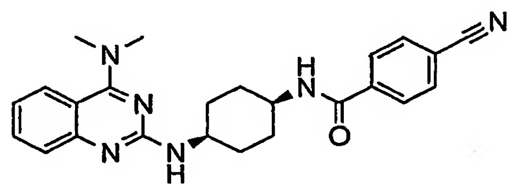
 ,

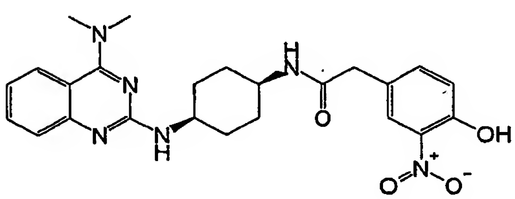
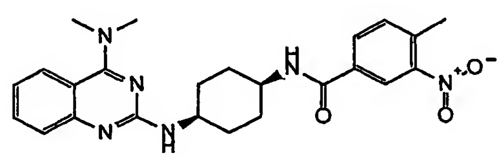
 ,

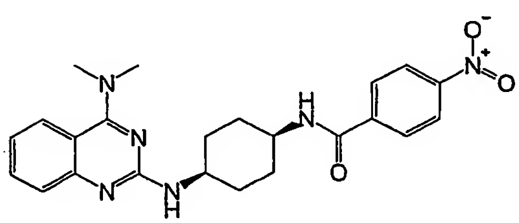
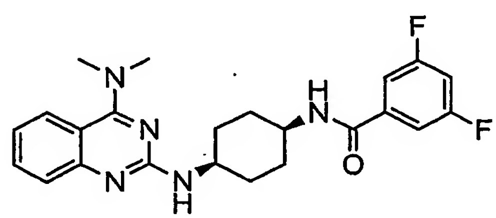
 ,

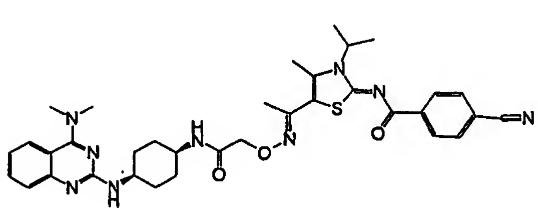
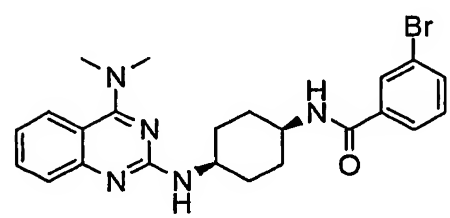

,

,

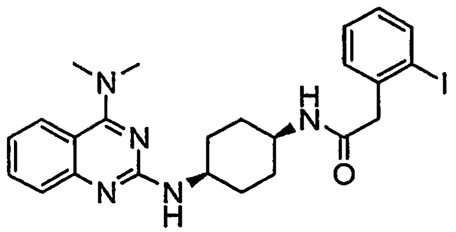
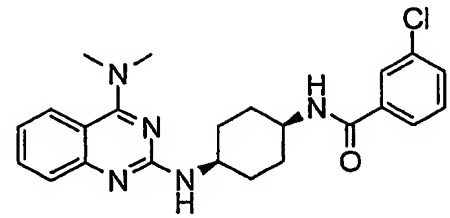

,

,

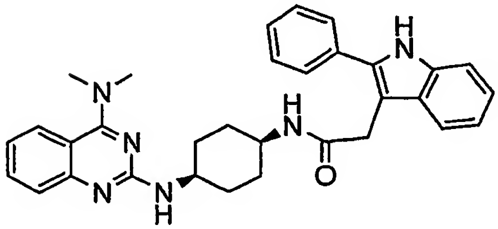
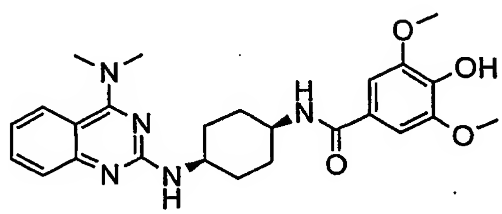

,

,

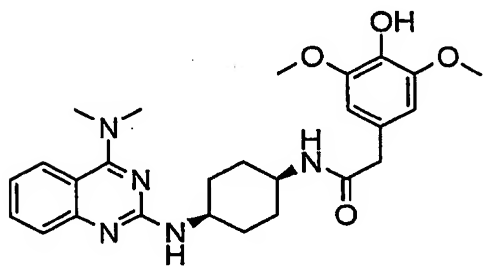
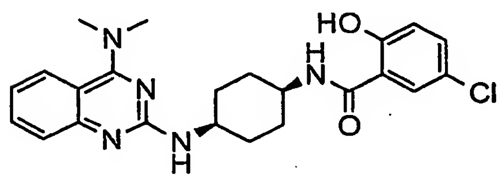

,

,

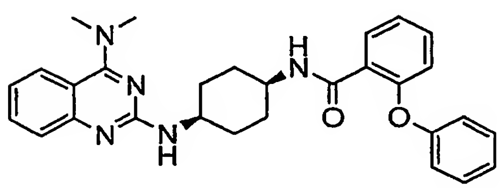
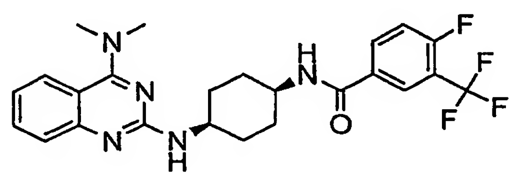

,

,

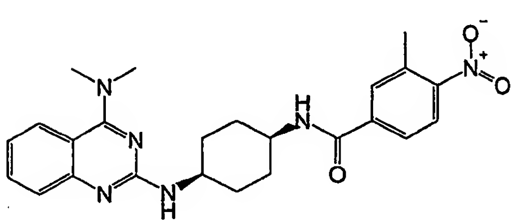
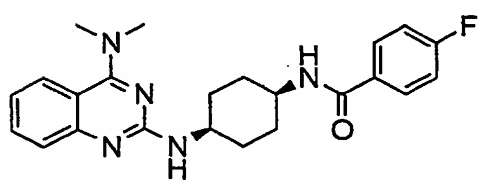

,

,

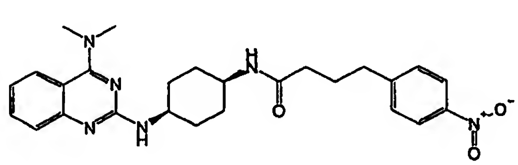
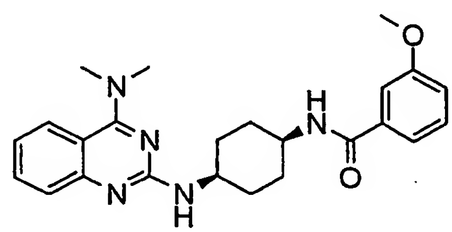

,

,

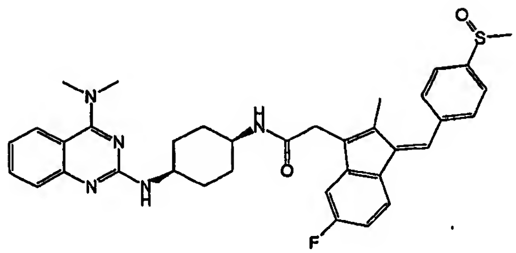
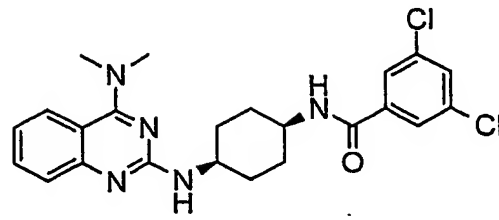

,

,

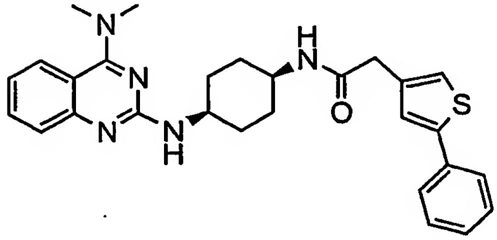
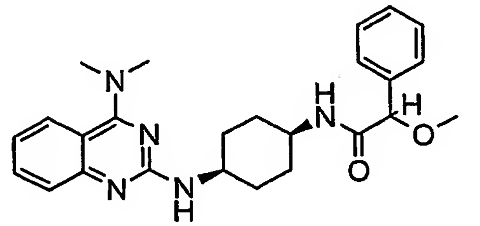

,

,

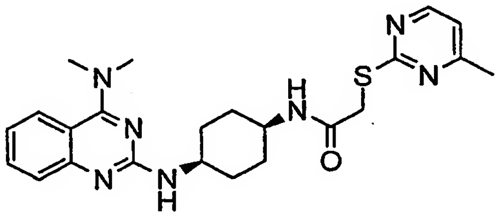
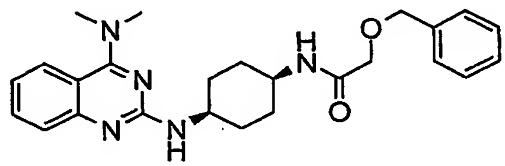

,

,

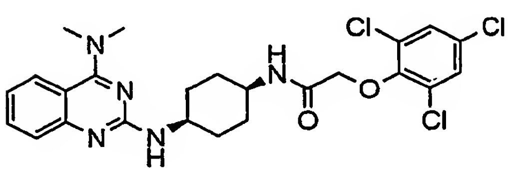
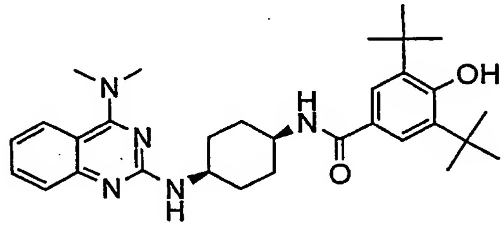

,

,

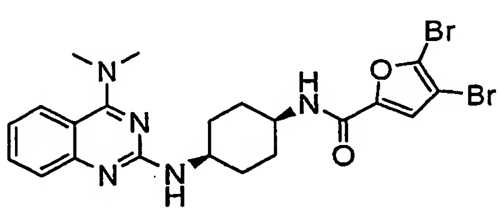
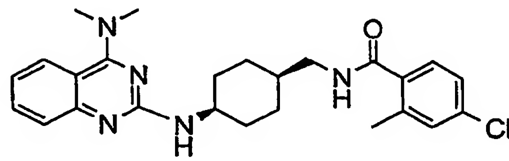

,

,

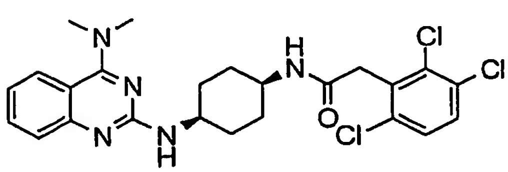
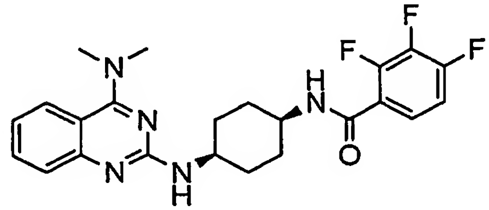
 ,  ,

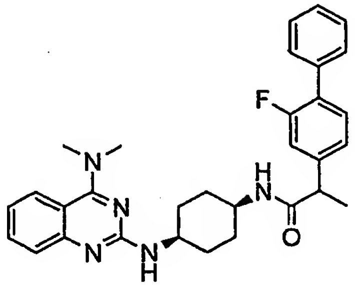
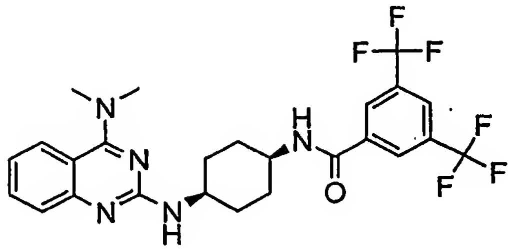
 ,  ,

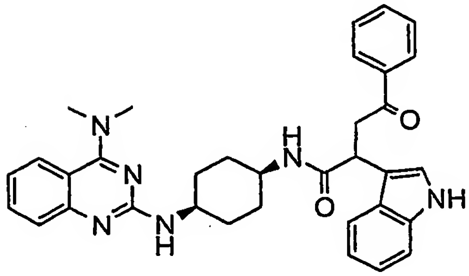
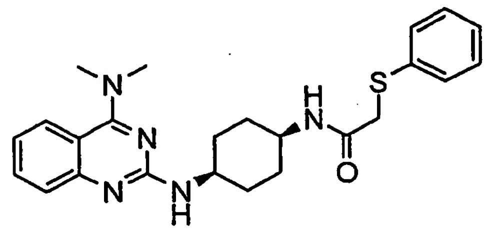
 ,  ,

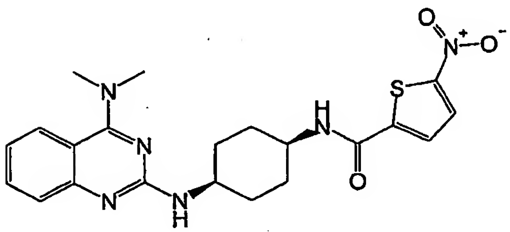
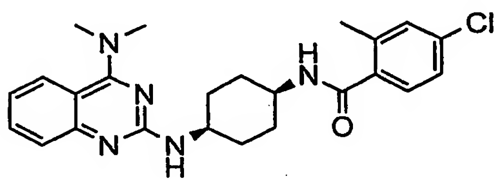
 ,  ,

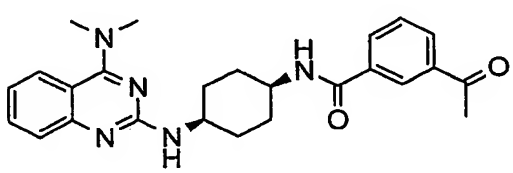
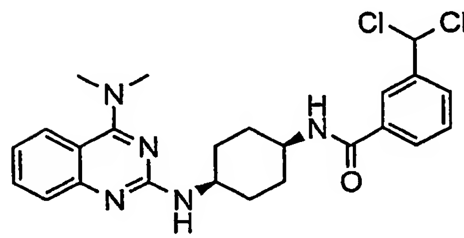
 ,  ,

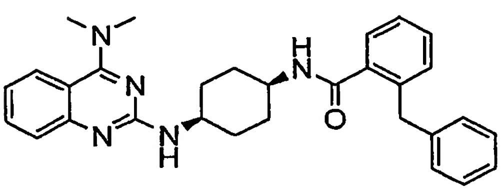
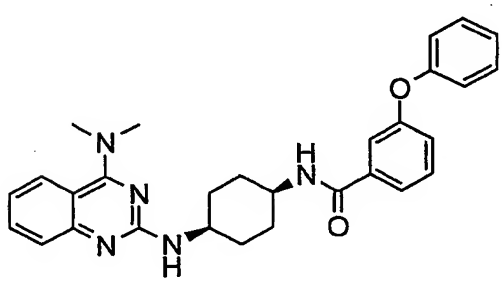
 ,  ,

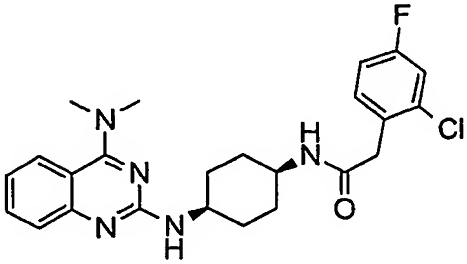
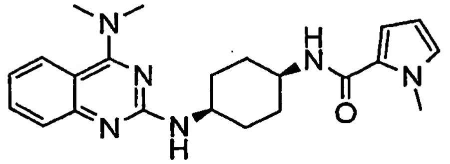

,

,

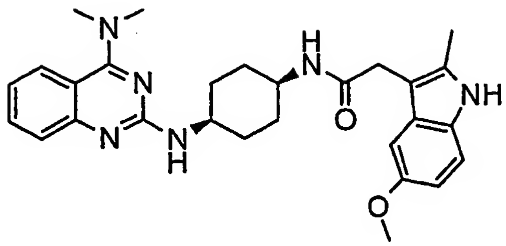
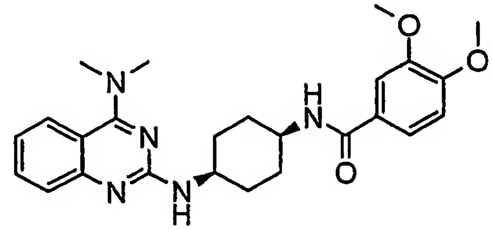

,

,

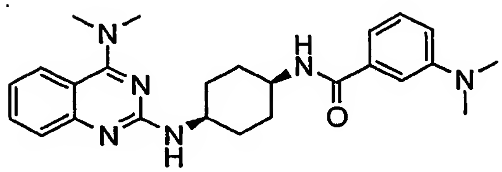
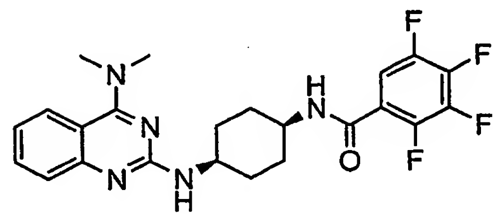

,

,

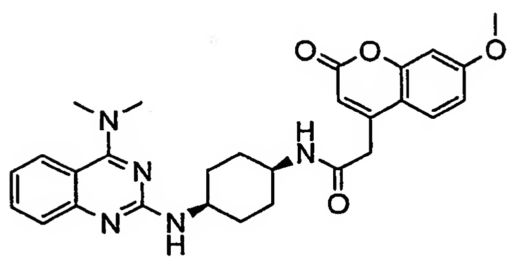
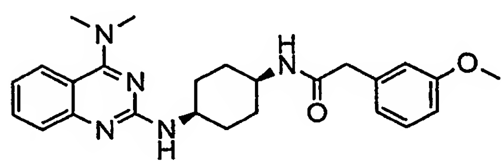

,

,

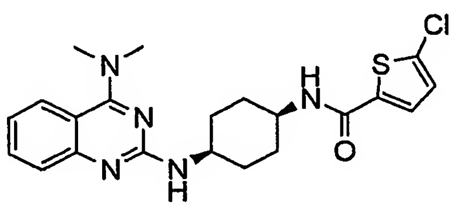
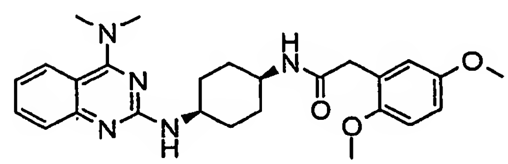

,

,

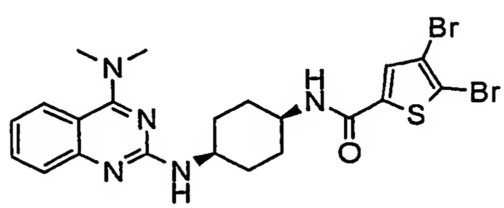
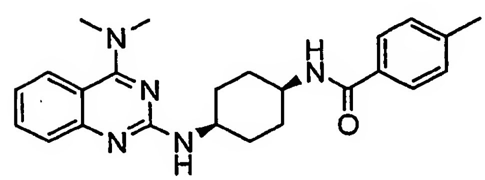

,

,

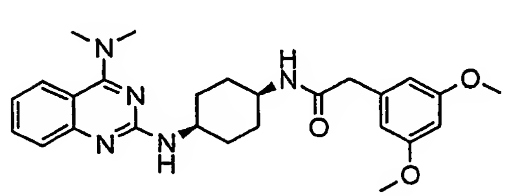
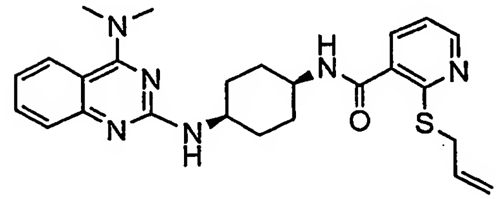
 ,  ,

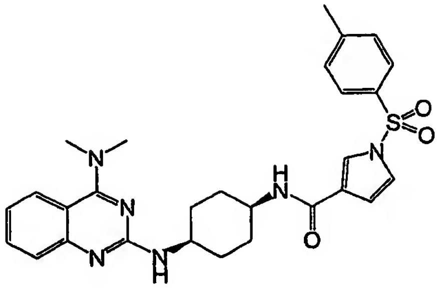
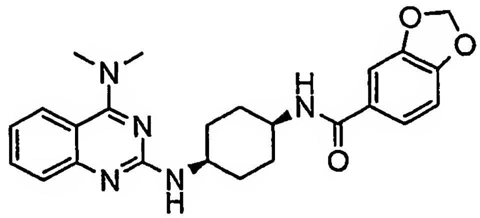
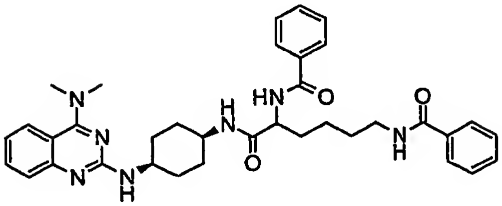
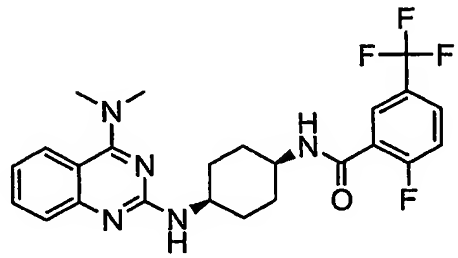
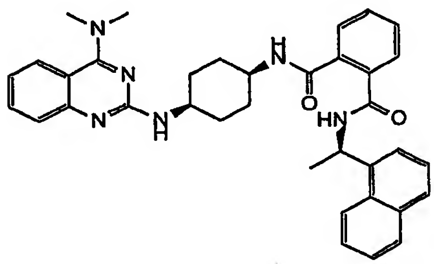
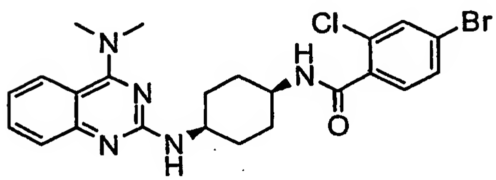
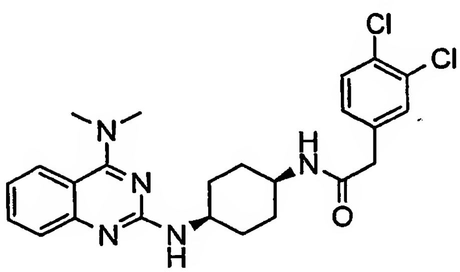
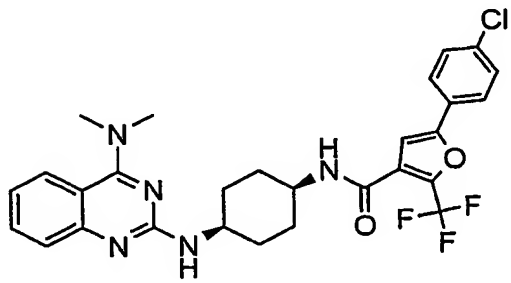
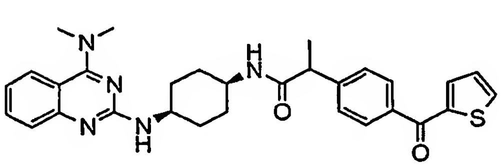
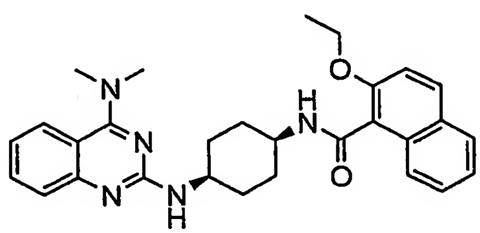
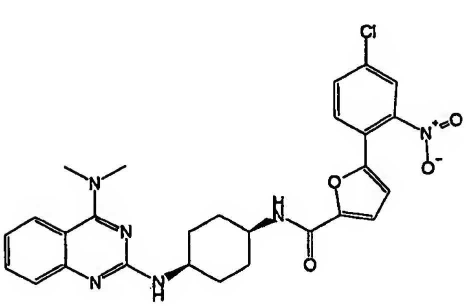
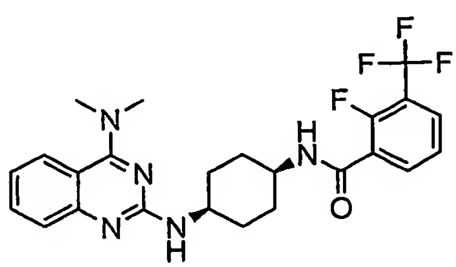
 ,  ,

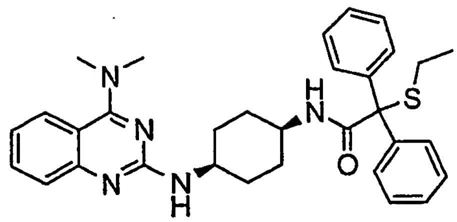
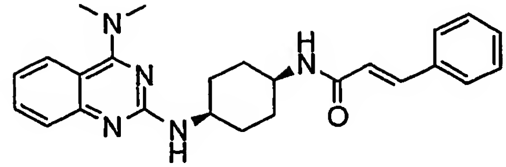
 ,  ,

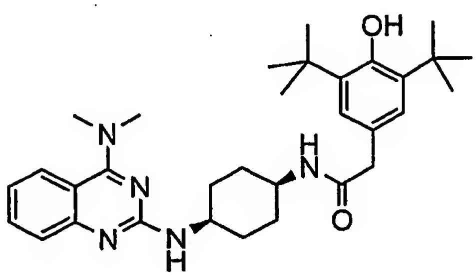
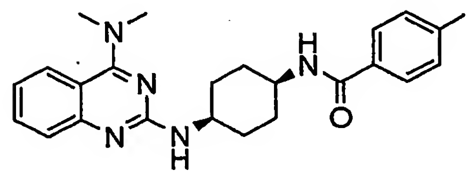
 ,  ,

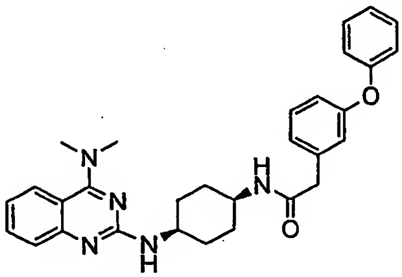
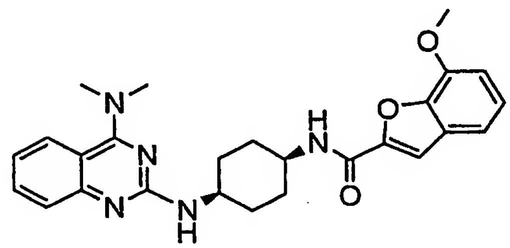
 ,  ,

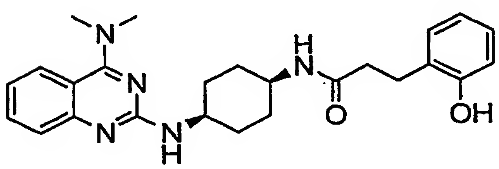
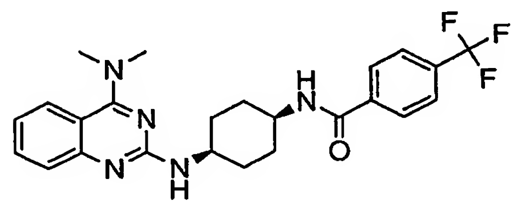
 ,  ,

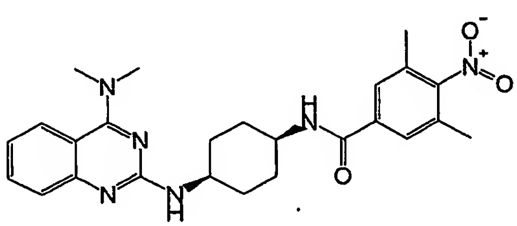
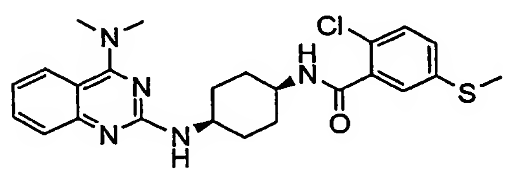

,

,

,

,

,

,

,

,

,

,

,

,

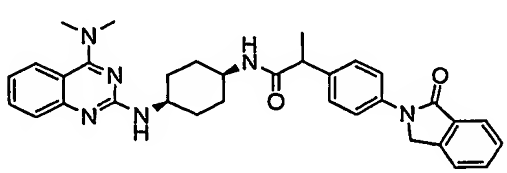
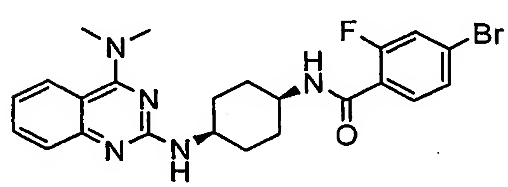
 ,  ,

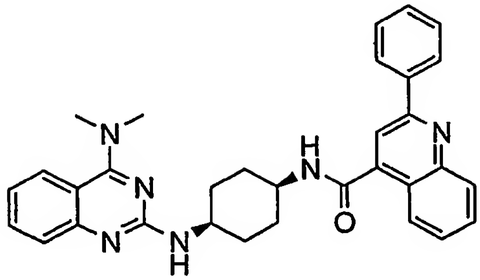
 ,  ,

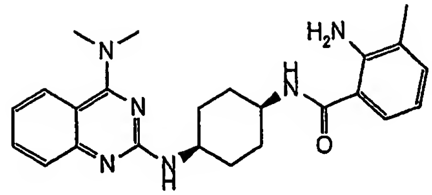
 ,  ,

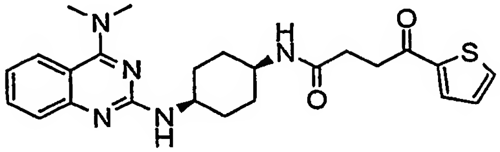
 ,  ,

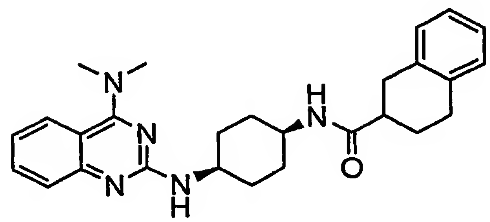
 ,  ,

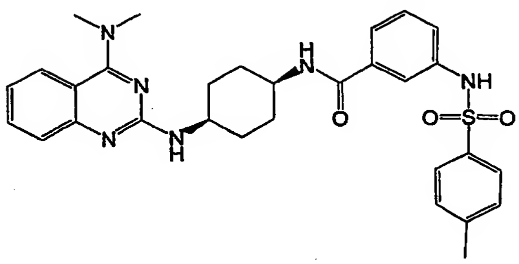
 ,  ,

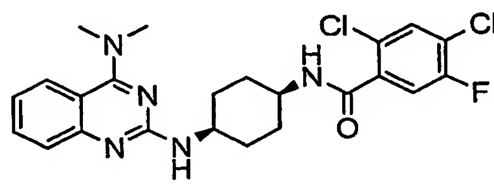
 ,

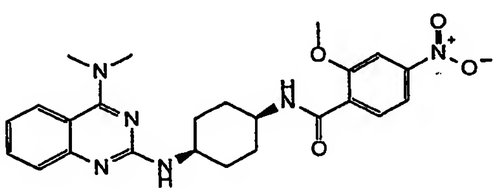
 ,

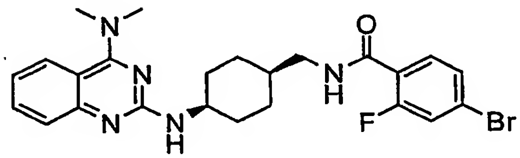
 ,

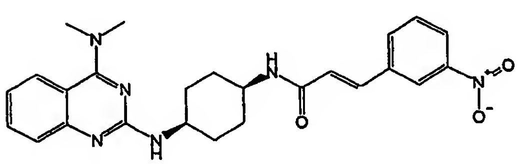
 ,

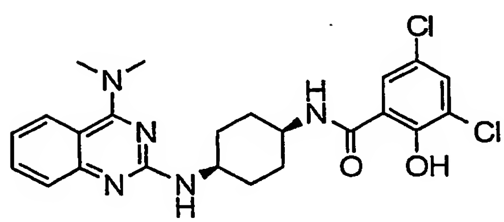
 ,

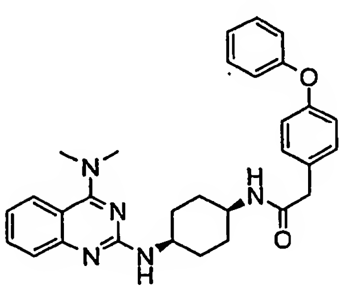
 ,

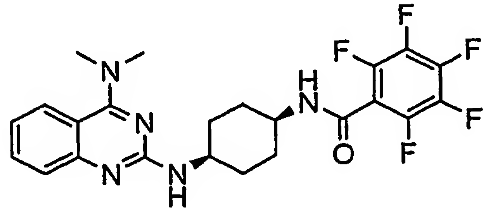
 ,

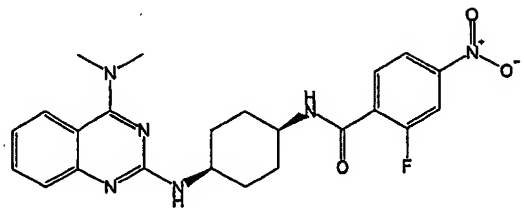
 ,

 ,

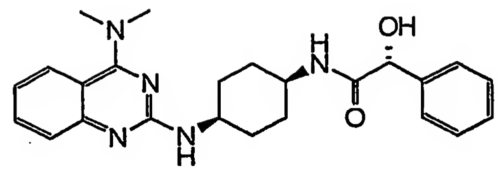
 ,

 ,

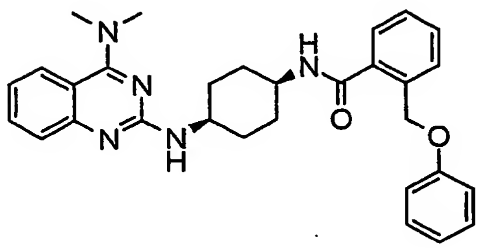
 ,



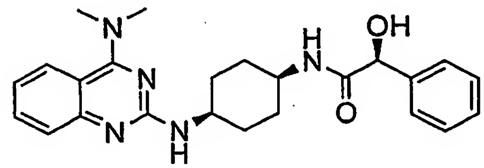
,



,



, and



; or, in case of, a salt thereof.

Other more preferred compounds of this invention are those compounds of Formula I wherein,

Q is Formula II;

R_1 represents

(i) C_1-C_{10} alkyl,

C_1-C_{10} alkyl substituted by substituent(s) independently selected from

•C_5-C_6 cycloalkyl,

•carbocyclic aryl,

•heterocyclyl,

(ii) C_3-C_6 cycloalkyl,

(iii) carbocyclic aryl,

(iv) or heterocyclyl;

R_2 is methylamino or dimethylamino;

L is selected from Formula XX - XXII;

Y is -C(O)-;

wherein carbocyclic aryl is phenyl, naphthyl, anthranyl, or biphenyl;

heterocyclyl is 1,3-dioxo-isoindolyl, 1*H*-indolyl, 1-oxo-3*H*-isobenzofuranyl, 2,3-dihydro-benzo[1,4]dioxinyl, 3,4-dihydro-2*H*-benzo[b][1,4]dioxepinyl, 4-oxo-3,4-dihydro-phthalazinyl, 9,10,10-trioxo-thioxanthenyl, 9*H*-xanthenyl, benzimidazolyl, benzo[1,3]dioxolyl, benzo[2,1,3]oxadiazolyl, benzo[b]thienyl, furyl, imidazolyl, isoxazolyl, morpholino, oxolanyl, piperidyl, pyridyl, quinoxalyl, thienyl, quinolyl, or benzothiazolyl;

halogen is fluoro, chloro, bromo, or iodo.

Further other more preferred compounds of this invention are those compounds of Formula I wherein,

Q is Formula II;

R_1 represents

(i) C_1-C_4 alkyl,

C_1-C_4 alkyl substituted by substituent(s) independently selected from

•cyclopentyl,

•carbocyclic aryl,

•heterocyclyl,

(ii) carbocyclic aryl,

(iii) or heterocyclyl;

R_2 is methylamino or dimethylamino;

L is selected from Formula XX - XXII;

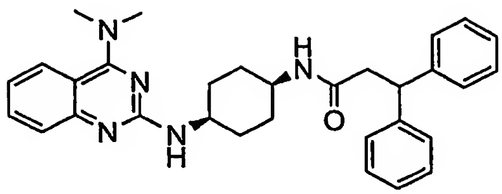
Y is -C(O)-;

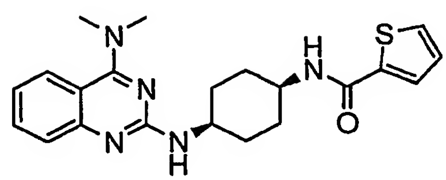
wherein carbocyclic aryl is phenyl, naphthyl, anthranyl, or biphenyl;

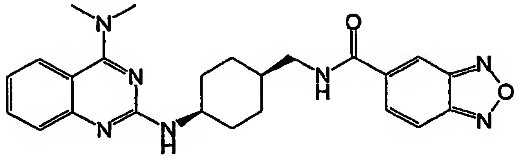
heterocyclyl is 9*H*-xanthenyl, benzo[1,3]dioxolyl, benzo[2,1,3]oxadiazolyl, benzo[b]thienyl, thienyl, 1*H*-indolyl, quinoxalyl, quinolyl, or benzothiazolyl;

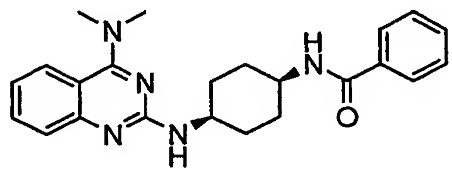
halogen is fluoro, chloro, bromo, or iodo.

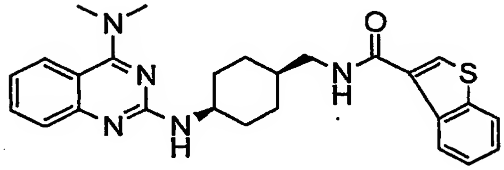
The following compounds are specially preffered;

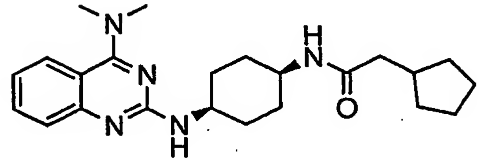
 ,

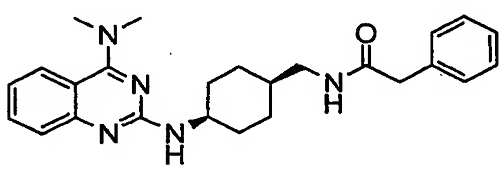
 ,

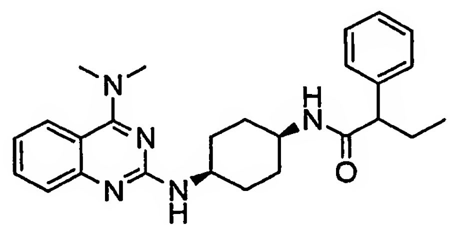
 ,

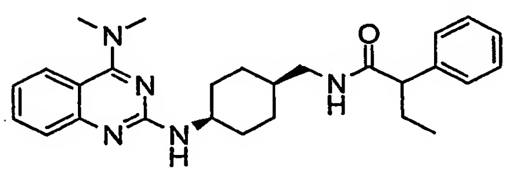
 ,

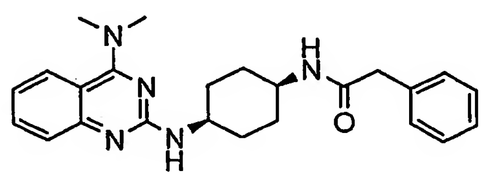
 ,

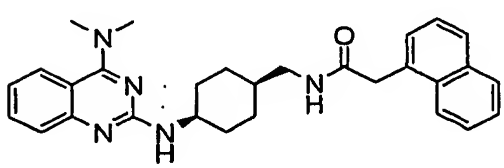
 ,

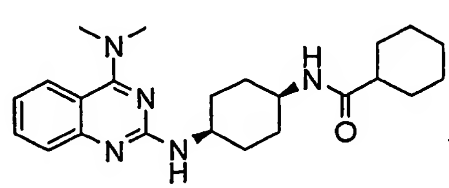
 ,

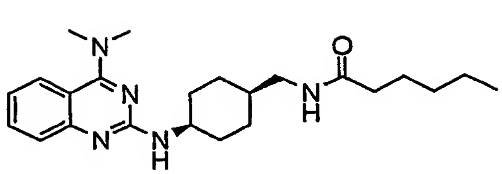
 ,

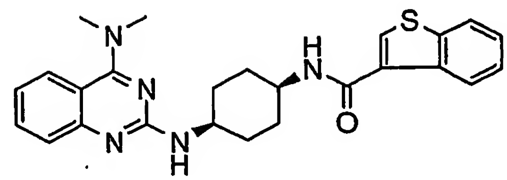
 ,

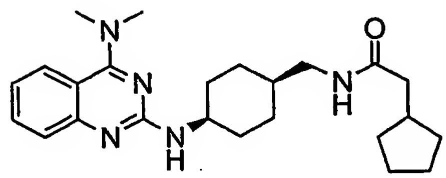
 ,

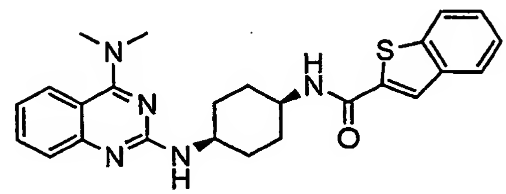
 ,

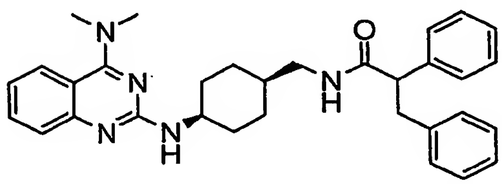
 ,

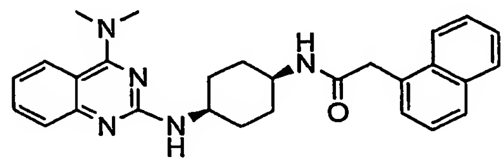
 ,

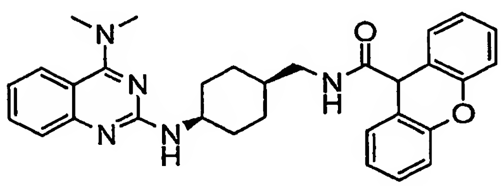
 ,

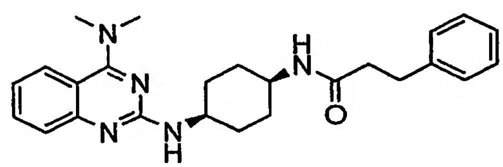
 ,

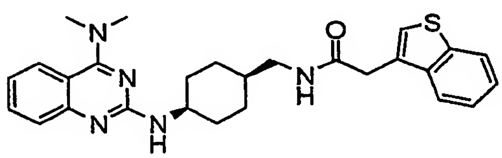
 ,

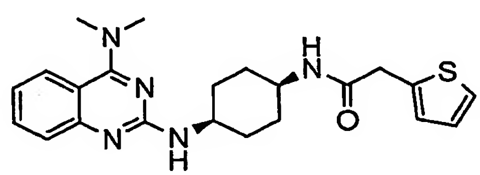
 ,

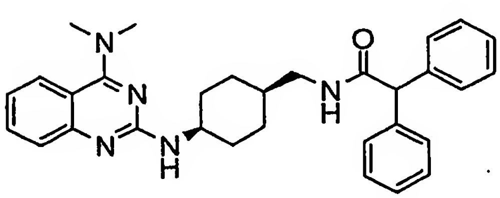
 ,

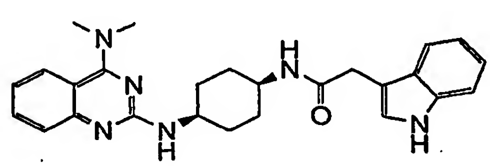
 ,

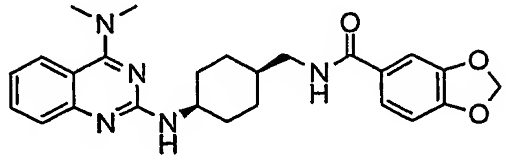
 ,

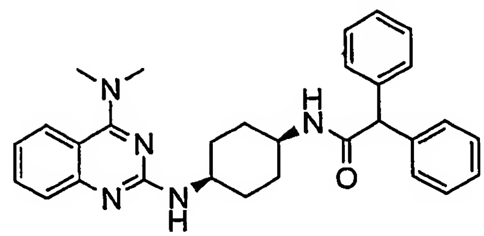
 ,

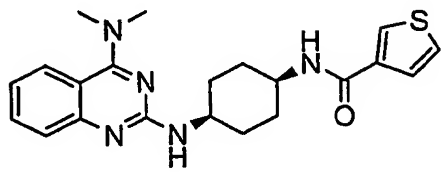
 ,

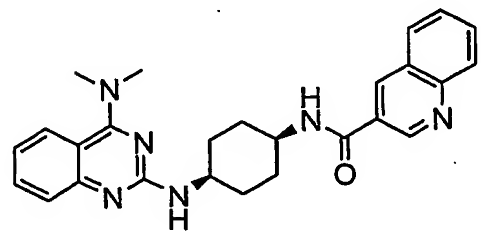
 ,

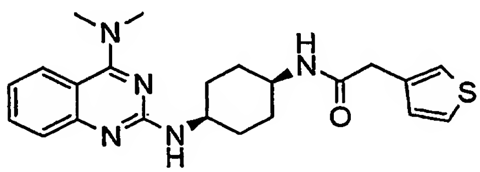
 ,

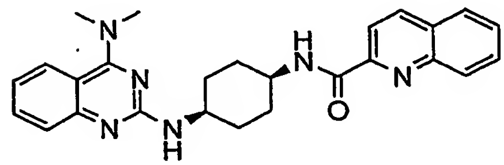
 ,

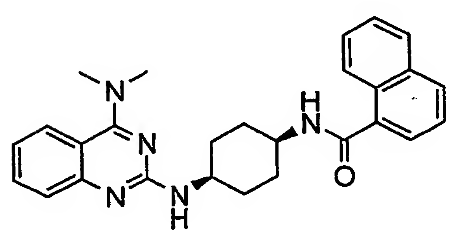
 ,

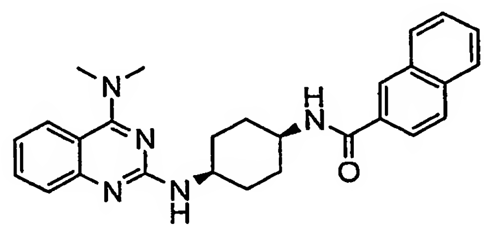
 ,

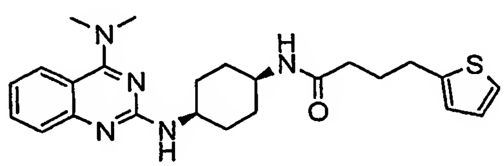
 ,

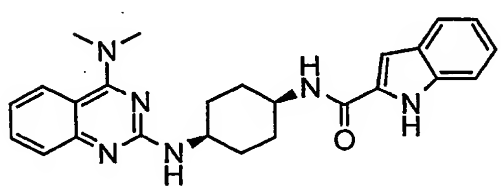
 ,

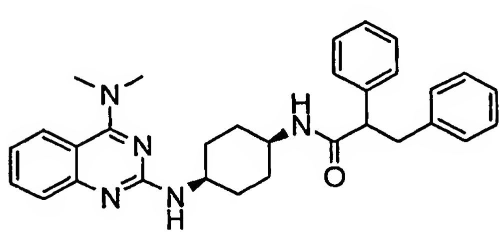
 ,

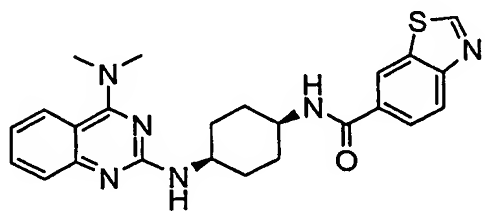
 ,

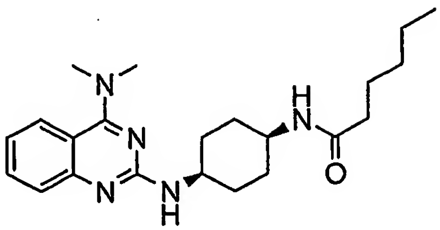
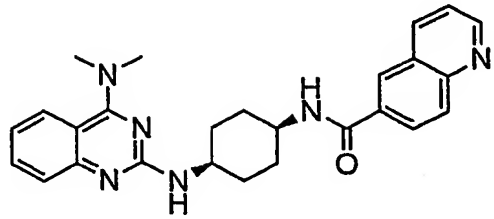
 ,

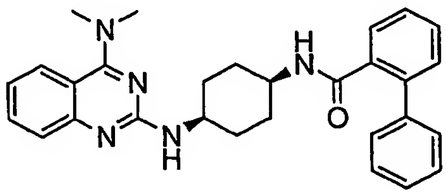
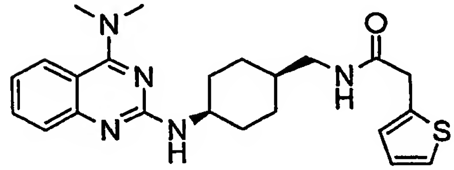
 ,

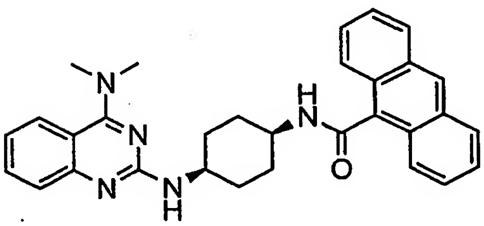
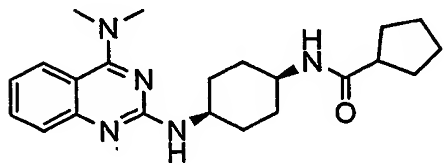
 ,

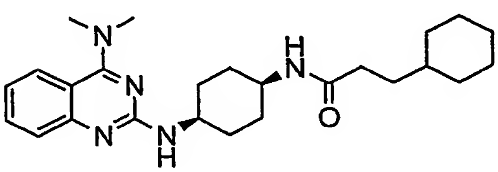
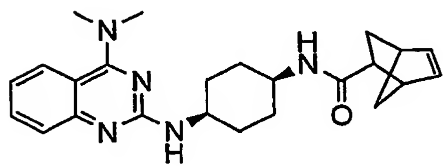
 ,

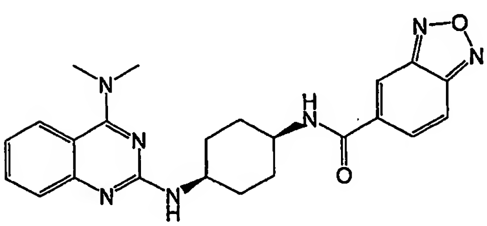
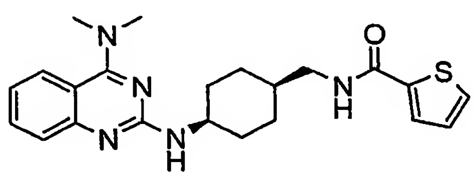
 ,

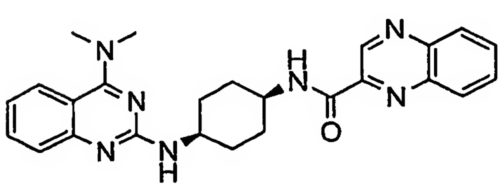
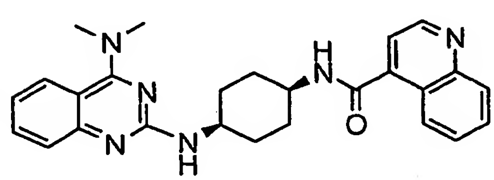
 ,  ,

 ,  ,

 ,  ,

 ,  ,

 ,  ,

 , and 

; or, in case of, a salt thereof.

Preferred compounds of this invention are those compounds of Formula I wherein,

Q is Formula II;

R_1 represents

(i) C_1-C_{10} alkyl,

C_1-C_{10} alkyl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•oxo,

•C_1-C_3 alkoxy,

•C_1-C_3 alkoxy substituted by substituent(s) independently selected from

••carbocyclic aryl,

••heterocyclyl,

••heterocyclyl substituted by C_1-C_3 alkyl,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by substituent(s) independently selected from

••halogen,

••nitro,

••carbocyclic aryl,

••carbocyclic aryl substituted by C_1-C_3 alkoxy,

••C_1-C_4 alkyl,

••C_1-C_4 alkyl substituted by substituent(s) independently selected from

•••mono- or di-C_1-C_3 alkylamino,

•••mono- or di-C_1-C_3 alkylamino substituted by carbocyclic aryl,

•••mono- or di-C_1-C_3 alkylamino substituted by halogenated carbocyclic aryl,

•mono- or di-C_1-C_3 alkylamino,

•mono- or di-C_1-C_3 alkylamino substituted by substituent(s) independently selected from

••cyano,

••carbocyclic aryl,

••heterocyclyl,

•mono- or di-carbocyclic arylamino,

•mono- or di-carbocyclic arylamino substituted by C_1-C_3 alkyl,

•C_1-C_3 alkylcalbonylamino,

•C_1-C_4 alkoxycalbonylamino,

•carbocyclic arylsulfonylamino,

•carbocyclic arylsulfonylamino substituted by substituent(s) independently selected from

••nitro,

••C_1-C_3 alkyl,

••mono- or di-C_1-C_3 alkylamino,

•C_1-C_3 alkylthio,

•C_1-C_3 alkylthio substituted by substituent(s) independently selected from

••mono- or di-carbocyclic arylamino,

••halogenated mono- or di-carbocyclic arylamino,

••carbocyclic aryl,

••carbocyclic aryl substituted by substituent(s) independently selected from

•••halogen,

•••C_1-C_3 alkoxy,

•carbocyclic arylthio,

•carbocyclic arylthio substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

•carbocyclic arylsulfonyl,

•halogenated carbocyclic arylsulfonyl,

•heterocyclylthio,

•C_3-C_6 cycloalkyl,

•C_3-C_6 cycloalkyl substituted by C_1-C_3 alkyl,

•carbocyclyl,

•carbocyclyl substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••C_2-C_3 alkenyl,

••C_2-C_3 alkenyl substituted by carbocyclic aryl,

••C_2-C_3 alkenyl substituted by carbocyclic aryl substituted C_1-C_3 alkylsulfinyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••nitro,

••C_1-C_4 alkyl,

••C_1-C_4 alkyl substituted by substituent(s) independently selected from

•••halogen,

•••hydroxy,

•••carbocyclic aryl,

•••mono- or di-carbocyclic arylamino,

•••mono- or di-carbocyclic arylamino substituted by substituent(s) independently selected from

••••halogen,

••••nitro,

••••C_1-C_3 alkyl,

••••C_1-C_3 alkoxy,

••••halogenated C_1-C_3 alkoxy,

••C_1-C_3 alkoxy,

••C_1-C_3 alkoxy substituted by substituent(s) independently selected from

•••halogen,

•••carbocyclic aryl,

••carbocyclic aryloxy,

••C_1-C_3 alkoxycarbonyl,

••mono- or di-C_1-C_3 alkylamino,

••C_1-C_3 alkylthio,

••halogenated C_1-C_3 alkylthio,

••C_1-C_3 alkylsulfonyl,

••C_3-C_6 cycloalkyl,

••carbocyclic aryl,

••heterocyclyl,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••C_1-C_3 alkoxy substituted by carbocyclic aryl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

(ii) C_2-C_8 alkenyl,

C_2-C_8 alkenyl substituted by substituent(s) independently selected from

•halogen,

•C_1-C_3 alkoxy,

•C_1-C_3 alkoxy substituted by carbocyclic aryl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••C_1-C_3 alkoxy,

••halogenated C_1-C_3 alkoxy,

•heterocyclyl,

•heterocyclyl substituted by nitro,

(iii) C_2-C_4 alkynyl,

C_2-C_4 alkynyl substituted by carbocyclic aryl,

(iv) C_3-C_6 cycloalkyl,

C_3-C_6 cycloalkyl substituted by substituent(s) independently selected from

•C_1-C_3 alkyl,

•C_1-C_3 alkyl substituted by substituent(s) independently selected from

••hydroxy,

••oxo,

••carbocyclic aryl,

•mono- or di-C_1-C_3 alkylamino,

•mono- or di-C_1-C_3 alkylamino substituted by carbocyclic aryl,

•carbocyclic aryl,

(v) C_3-C_6 cycloalkeyl,

C_3-C_6 cycloalkeyl substituted by C_1-C_3 alkyl,

(vi) carbocyclyl,

carbocyclyl substituted by substituent(s) independently selected from

•hydroxy,

•nitro,

(vii) carbocyclic aryl,

carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•cyano,

•nitro,

•C_1-C_9 alkyl,

•C_1-C_9 alkyl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••oxo,

••C_1-C_3 alkoxy,

••carbocyclic aryloxy,

••mono- or di-C_1-C_3 alkylamino-N-oxy,

••mono- or di-C_1-C_3 alkylamino,

••mono- or di-C_1-C_3 alkylamino substituted by carbocyclic aryl,

••mono- or di-carbocyclic arylamino,

••mono- or di-carbocyclic arylamino substituted by C_1-C_3 alkoxy,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

••heterocyclyl,

••heterocyclyl substituted by C_1-C_3 alkyl,

•C_2-C_3 alkenyl,

•C_2-C_3 alkenyl substituted by carbocyclic aryl,

•C_1-C_9 alkoxy,

•C_1-C_9 alkoxy substituted by substituent(s) independently selected from

••hydroxy,

••halogen,

••carboxy,

••mono- or di-C_1-C_3 alkylamino,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

••heterocyclyl,

••heterocyclyl substituted by substituent(s) independently selected from

•••heterocyclyl,

•••heterocyclyl substituted by substituent(s) independently selected from

••••halogen,

••••C_1-C_3 alkyl,

••••halogenated C_1-C_3 alkyl,

•C_2-C_3 alkenyloxy,

•C_1-C_3 alkylcarbonyloxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by substituent(s) independently selected from

••halogen,

••C_1-C_4 alkyl,

••halogenated C_1-C_4 alkyl,

••C_1-C_3 alkoxy,

•heterocyclyloxy,

•heterocyclyloxy substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl,

•(carbocyclic aryl)$S(O)_2O$,

•carboxy,

•C_1-C_3 alkoxycarbonyl,

•mono- or di-C_1-C_3 alkylaminocarbonyl,

•mono- or di-C_1-C_3 alkylaminocarbonyl substituted by carbocyclic aryl,

•amino,

•mono- or di-C_1-C_4 alkylamino,

•mono- or di-C_1-C_4 alkylamino substituted by cyano,

•mono- or di-carbocyclic arylamino,

•C_1-C_3 alkylcarbonylamino,

•carbocyclic arylsulfonylamino,

•carbocyclic arylsulfonylamino substituted by C_1-C_3 alkyl,

•(carbocyclic aryl)NHC(O)NH,

•(carbocyclic aryl)NHC(O)NH substituted by C_1-C_3 alkoxy,

•(carbocyclic aryl)NHC(O)NH substituted by haloganated C_1-C_3 alkoxy,

•C_1-C_3 alkylthio,

•halogenated C_1-C_3 alkylthio,

•carbocyclic arylthio,

•halogenated carbocyclic arylthio,

•carbocyclic arylthio substituted by C_1-C_3 alkyl,

•heterocyclylthio,

•C_1-C_3 alkylsulfonyl,

•mono- or di-C_1-C_3 alkylaminosulfonyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••C_1-C_7 alkyl,

••halogenated C_1-C_7 alkyl,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••C_1-C_3 alkyl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

(viii) heterocyclyl,

or heterocyclyl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•cyano,

•nitro,

•C_1-C_4 alkyl,

•C_1-C_4 alkyl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••oxo,

••C_1-C_3 alkylcarbonyloxy,

••C_1-C_3 alkoxycarbonyl,

••C_1-C_3 alkylthio,

••C_1-C_3 alkylthio substituted by carbocyclic aryl,

••C_1-C_3 alkylthio substituted by halogenated carbocyclic aryl,

••carbocyclic aryl,

••carbocyclic aryl substituted by substituent(s) independently selected from

•••halogen,

•••nitro,

••heterocyclyl,

•C_1-C_3 alkoxy,

•C_1-C_3 alkoxy substituted by carbocyclic aryl,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by C_1-C_3 alkyl,

•mono- or di-C_1-C_3 alkylamino,

•C_1-C_4 alkylcarbonylamino,

•C_1-C_3 alkylthio,

•carbocyclic arylthio,

•halogenated carbocyclic arylthio,

•carbocyclic arylthio substituted by C_1-C_3 alkoxycarbonyl,

•heterocyclylthio,

•heterocyclylthio substituted by C_1-C_3 alkyl,

•C_1-C_3 alkylsulfonyl,

•carbocyclic arylsulfonyl,

•carbocyclic arylsulfonyl substituted by C_1-C_4 alkyl,

•C_1-C_3 alkoxycarbonyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••nitro,

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••halogenated C_1-C_3 alkoxy,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••C_1-C_3 alkoxycarbonyl;

R_2 is $-NHNH_2$, -NHNHBoc, $-N(R_{2a})(R_{2b})$, morpholino, 4-acetyl-piperazyl, or 4-phenyl-piperazyl;

wherein R_{2a} is H or C_1-C_3 alkyl;

R_{2b} is C_1-C_4 alkyl, C_1-C_4 alkyl substituted by substituent(s) independently selected from

•hydroxy,

•C_1-C_3 alkoxy,

•amino,

•-NHBoc,

•C_3-C_6 cycloalkyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••$-SO_2NH_2$,

•heterocyclyl,

C_3-C_6 cycloalkyl, carbocyclic aryl, carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•C_1-C_3 alkyl,

•C_1-C_3 alkoxy,

or a group of Formula IV;

wherein Boc is carbamic acid *tert*-butyl ester and R_3 is C_1-C_3 alkyl or C_1-C_3 alkyl substituted by substituent(s) independently selected from

•carbocyclic aryl,

•halogenated carbocyclic aryl,

•carbocyclic aryl substituted by C_1-C_3 alkoxy;

L is selected from Formula V - XIX;

wherein R_4 is H or C_1-C_3 alkyl;

R_5 is H, C_1-C_3 alkyl, or C_1-C_3 alkyl substituted by a substituted carbocyclic aryl;

Y is -$(CH_2)_m$, m is 0 or 1;

wherein carbocyclic aryl is phenyl, naphthyl, phenanthryl, or biphenyl;

carbocyclyl is 9*H*-fluorenyl, 9-oxo-fluorenyl, acenaphthyl, anthraquinonyl, indanyl, or indenyl;

heterocyclyl is 1,2,3-thiadiazolyl, 1,2,3-triazolyl, 1,2-dihydro-3-oxo-pyrazolyl, 1,3,4-thiadiazolyl, 1,3-dioxo-isoindolyl, 1,3-dioxolanyl, 1*H*-indolyl, 1*H*-pyrrolo[2,3-c]pyridyl, 1*H*-pyrrolyl, 2,2',5',2"-terthiophenyl, 2,2'-bithiophenyl, 2,3-dihydro-1-oxo-isoindolyl, 2,3-dihydro-benzo[1,4]dioxinyl, 2,3-dihydro-benzofuryl, 2,4-dihydro-3-oxo-pyrazolyl, 2*H*-benzopyranyl, 2-oxo-pyrrolidinyl, 3,4-dihydro-2*H*-benzo[1,4]oxazinyl, 3,4-dihydro-2*H*-benzo[b][1,4]dioxepinyl, 4*H*-benzo[1,3]dioxinyl, 4*H*-benzopyranyl, 4-oxo-1,5,6,7-tetrahydro-indolyl, 4-oxo-benzopyranyl, 9*H*-carbazolyl, 9*H*-xanthenyl, azetidinyl, benzimidazolyl, benzo[1,3]dioxolyl, benzo[b]thienyl, benzofuryl, benzothiazolyl, furyl, imidazo[2,1-b]thiazolyl, imidazolyl, isoxazolyl, morpholino, morpholinyl, oxolanyl, piperazyl, piperidyl, pyrazolo[5,1-b]thiazolyl, pyrazolyl, pyridyl, pyrimidyl, pyrrolidyl, quinolyl, quinoxalyl, thiazolidyl, thiazolyl, thienyl, or thiolanyl;

halogen is fluoro, chloro, bromo, or iodo.

Other preferred compounds of this invention are those compounds of Formula I wherein,

Q is Formula II;

R_1 represents

(i) C_1-C_{10} alkyl substituted by substituent(s) independently selected from

•methoxy,

•methoxy substituted by carbocyclic aryl,

•carbocyclic aryloxy,

•halogenated carbocyclic aryloxy,

•mono-C_1-C_2 alkylamino substituted by cyano,

•mono- or di-C_1-C_2 alkylamino substituted by carbocyclic aryl,

•mono-carbocyclic arylamino,

•mono-carbocyclic arylamino substituted by methyl,

•carbocyclic arylsulfonylamino substituted by methyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••nitro,

••C_1-C_4 alkyl,

••C_1-C_4 alkyl substituted by carbocyclic aryl,

••C_1-C_4 alkyl substituted by hydroxy,

••C_1-C_2 alkoxy,

••halogenated C_1-C_2 alkoxy,

•heterocyclyl substituted by carbocyclic aryl,

(ii) C_2-C_8 alkenyl substituted by substituent(s) independently selected from

•methoxy substituted by carbocyclic aryl,

•carbocyclic aryl,

•carbocyclic aryl substituted by methoxy,

(iii) C_2-C_4 alkynyl substituted by carbocyclic aryl,

(iv) cyclohexyl substituted by carbocyclic arylmethyl,

(v) carbocyclyl,

(vi) carbocyclic aryl,

carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•cyano,

•amino,

•C_1-C_9 alkyl,

•halogenated C_1-C_9 alkyl,

•C_1-C_9 alkoxy,

•C_1-C_9 alkoxy substituted by substituent(s) independently selected from

••halogen,

••halogenated carbocyclic aryl,

•propenyloxy,

•methylamino,

•di-C_1-C_2 alkylamino,

•di-C_1-C_2 alkylamino substituted by cyano,

•methylthio,

•halogenated methylthio,

(vii) heterocyclyl,

or heterocyclyl substituted by substituent(s) independently selected from

•halogen,

•C_1-C_4 alkyl,

•C_1-C_4 alkyl substituted by hydroxy,

•C_1-C_4 alkyl substituted by carbocyclic aryl,

•methoxy,

•C_1-C_2 alkoxycarbonyl,

•carbocyclic arylthio substituted by methoxycarbonyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••halogenated methyl,

•heterocyclyl;

R_2 is methylamino or dimethylamino;

L is selected from Formula Va, VIIIa, or IXa;

wherein R_4 and R_5 are independently selected from H or C_1-C_3 alkyl;

Y is -$(CH_2)_m$, m is 0 or 1;

wherein carbocyclic aryl is phenyl, naphthyl, phenanthryl, or biphenyl;

carbocyclyl is 9*H*-fluorenyl, acenaphthyl, or anthraquinonyl;

heterocyclyl is 1,2,3-thiadiazolyl, 1,2,3-triazolyl, 1,2-dihydro-3-oxo-pyrazolyl, 1,3-dioxolanyl, 1*H*-indolyl, 1*H*-pyrrolyl, 2,2',5',2"-terthiophenyl, 2,2'-bithiophenyl, 2,3-

dihydro-benzo[1,4]dioxinyl, 3,4-dihydro-2*H*-benzo[1,4]oxazinyl, 4-oxo-benzopyranyl, 9*H*-carbazolyl, 9*H*-xanthenyl, benzimidazolyl, benzo[1,3]dioxolyl, benzo[b]thienyl, benzofuryl, benzothiazolyl, furyl, imidazolyl, isoxazolyl, oxolanyl, pyrazolo[5,1-b]thiazolyl, pyrazolyl, pyridyl, pyrimidyl, quinolyl, quinoxalyl, thiazolidyl, thiazolyl, thienyl, 2*H*-benzopyranyl, 4*H*-benzo[1,3]dioxinyl, azetidinyl, imidazo[2,1-b]thiazolyl, morpholinyl, or 2,3-dihydro-benzofuryl;

halogen is fluoro, chloro, bromo, or iodo.

Other more preferred compounds of this invention are those compounds of Formula I wherein,

Q is Formula II;

R_1 represents

(i) C_1-C_7 alkyl substituted by substituent(s) independently selected from

•methoxy,

•methoxy substituted by carbocyclic aryl,

•carbocyclic aryloxy,

•halogenated carbocyclic aryloxy,

•mono-ethylamino substituted by cyano,

•di-methylamino substituted by carbocyclic aryl,

•mono-carbocyclic arylamino,

•mono-carbocyclic arylamino substituted by methyl,

•carbocyclic arylsulfonylamino substituted by methyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••nitro,

••C_1-C_4 alkyl,

••C_1-C_4 alkyl substituted by carbocyclic aryl,

••C_1-C_4 alkyl substituted by hydroxy,

••metoxy,

••halogenated methoxy,

•heterocyclyl substituted by carbocyclic aryl,

(ii) C_2-C_7 alkenyl substituted by substituent(s) independently selected from

•methoxy substituted by carbocyclic aryl,

•carbocyclic aryl,

•carbocyclic aryl substituted by methoxy,

(iii) butynyl substituted by carbocyclic aryl,

(iv) cyclohexyl substituted by carbocyclic arylmethyl,

(v) carbocyclyl,

(vi) carbocyclic aryl,

carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•cyano,

•amino,

•C_1-C_2 alkyl,

•halogenated methyl,

•C_1-C_3 alkoxy,

•C_1-C_3 alkoxy substituted by substituent(s) independently selected from

••halogen,

••halogenated carbocyclic aryl,

•propenyloxy,

•di-C_1-C_2 alkylamino,

•di-C_1-C_2 alkylamino substituted by cyano,

•methylthio,

•halogenated methylthio,

(vii) heterocyclyl,

or heterocyclyl substituted by substituent(s) independently selected from

•halogen,

•C_1-C_3 alkyl,

•C_1-C_3 alkyl substituted by hydroxy,

•C_1-C_3 alkyl substituted by carbocyclic aryl,

•methoxy,

•ethoxycarbonyl,

•carbocyclic arylthio substituted by methoxycarbonyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••halogenated methyl,

•heterocyclyl;

R_2 is methylamino or dimethylamino;

L is selected from Formula XX - XXII;

Y is $-(CH_2)_m$, m is 0 or 1;

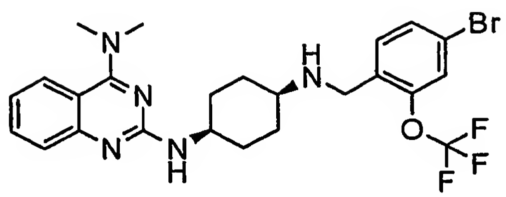
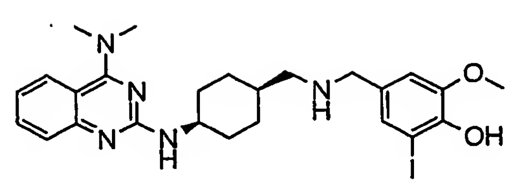
wherein carbocyclic aryl is phenyl, **naphthyl**, or biphenyl;

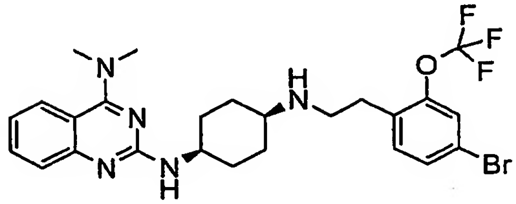
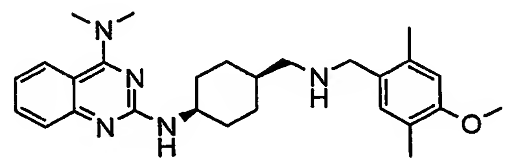
carbocyclyl is acenaphthyl;

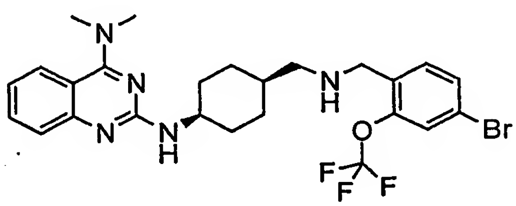
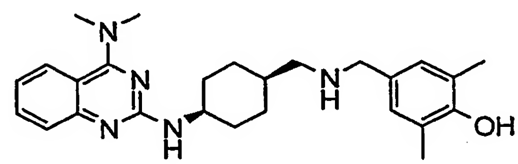
heterocyclyl is 1*H*-indolyl, 1*H*-pyrrolyl, 2,3-dihydro-benzo[1,4]dioxinyl, 9*H*-carbazolyl, benzo[1,3]dioxolyl, furyl, pyrazolyl, thienyl, 4-oxo-benzopyranyl, azetidinyl, imidazo[2,1-b]thiazolyl, pyridyl, imidazolyl, 2,3-dihydro-benzofuryl, or benzo[b]thienyl;;

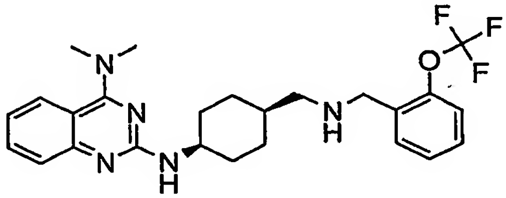
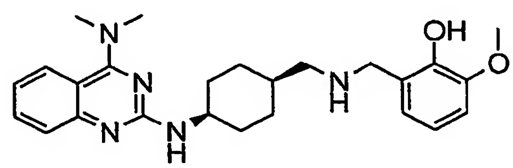
halogen is fluoro, chloro, bromo, or iodo.

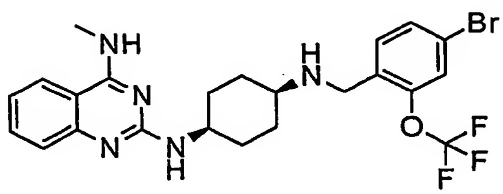
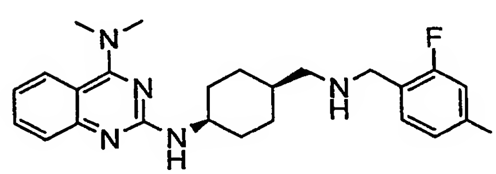
The following compounds are specially preffered;

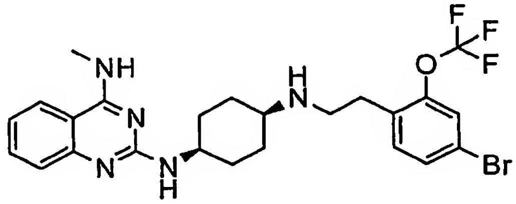
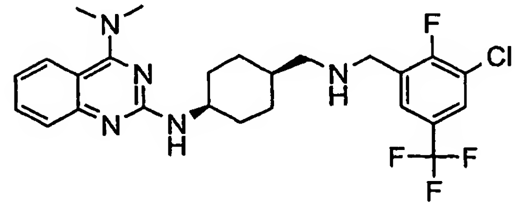
 ,  ,

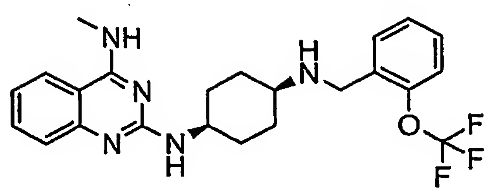
 ,  ,

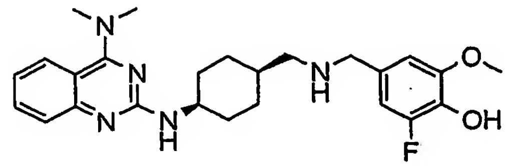
 ,  ,

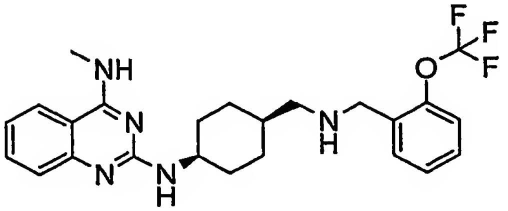
 ,  ,

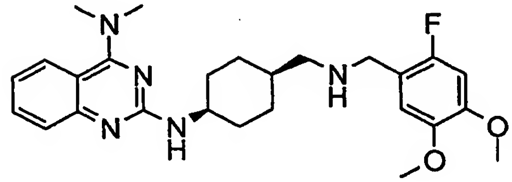
 ,  ,

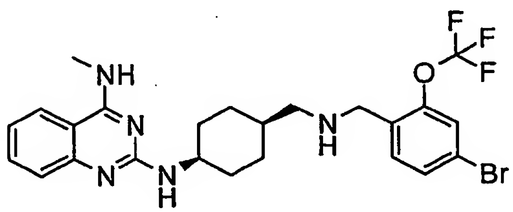
 ,  ,

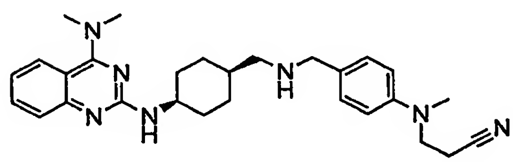
 ,

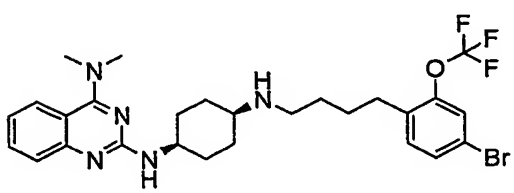
 ,

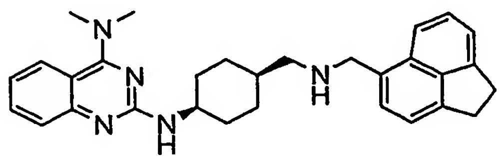
 ,

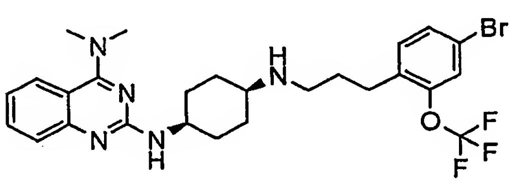
 ,

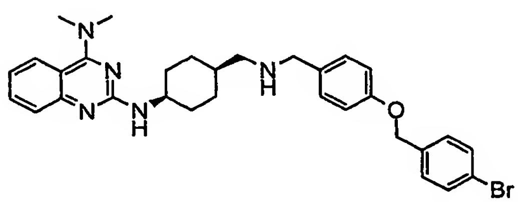
 ,

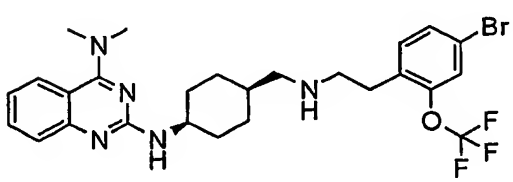
 ,

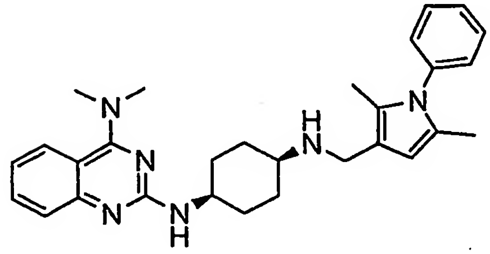
 ,

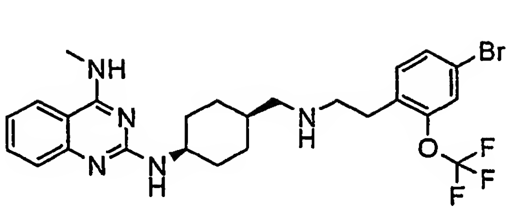
 ,

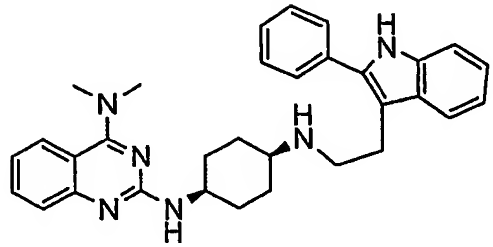
 ,

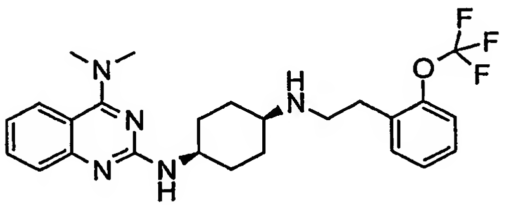
 ,

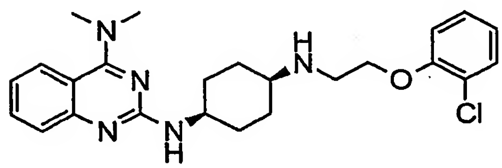
 ,

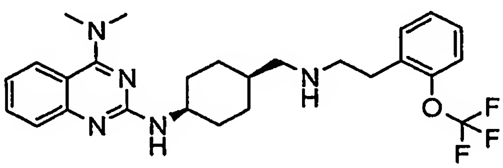
 ,

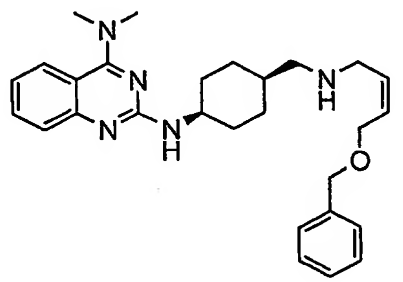
 ,

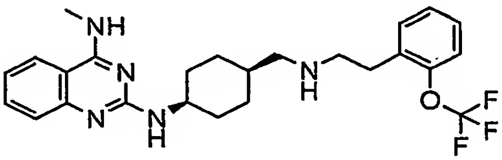
 ,

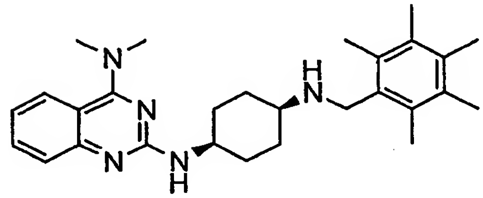
 ,

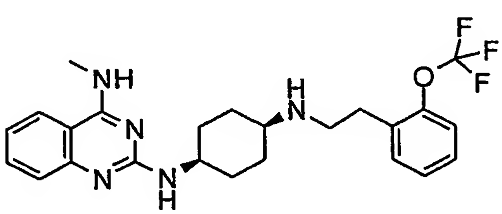
 ,

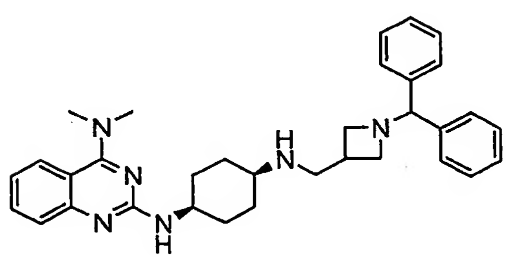
 ,

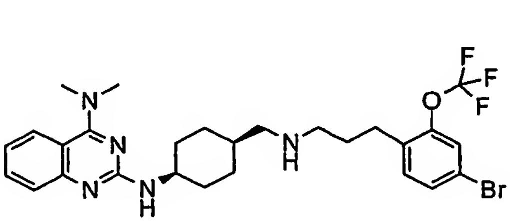
 ,

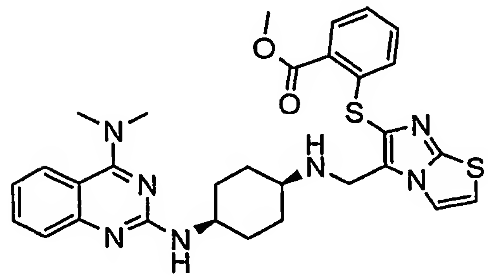
 ,

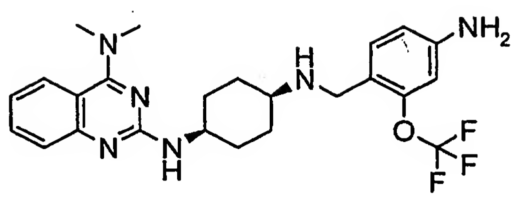
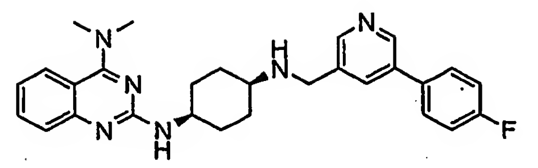
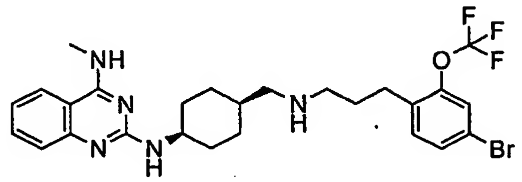
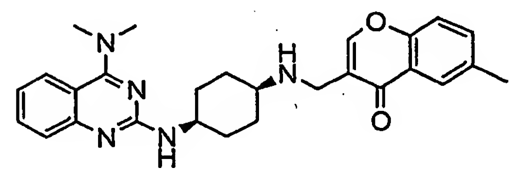
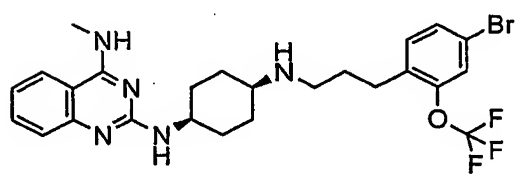
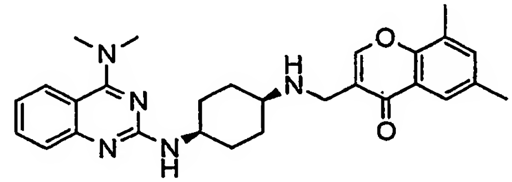
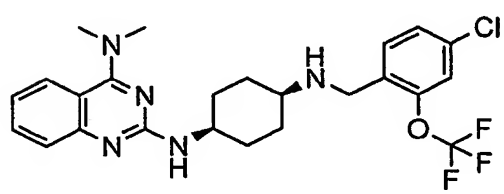
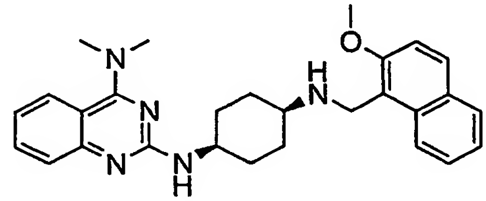
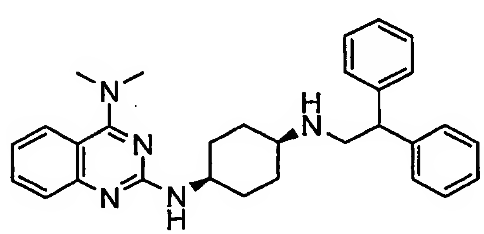
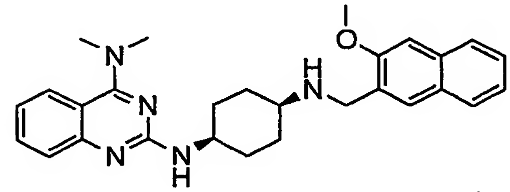
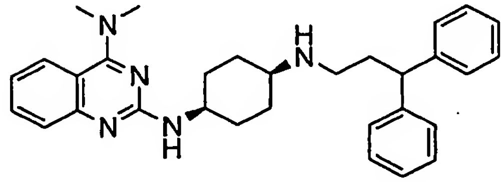
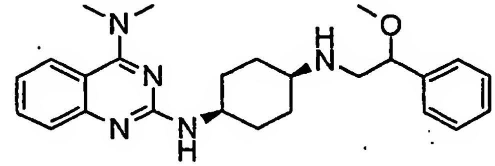
 ,

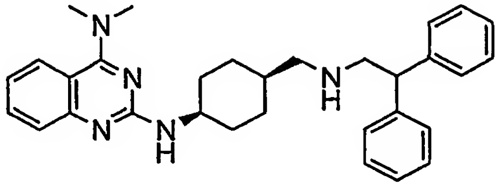
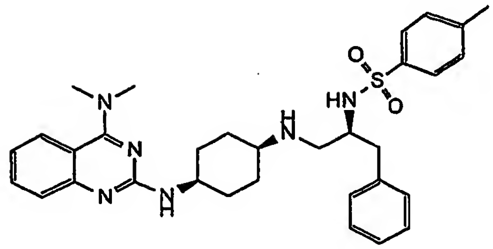
 ,

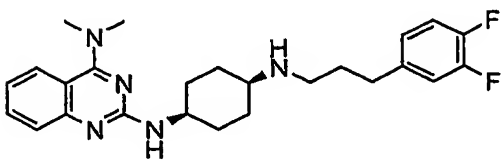
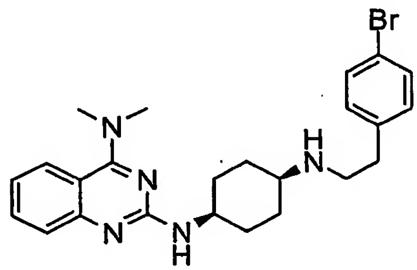
 ,

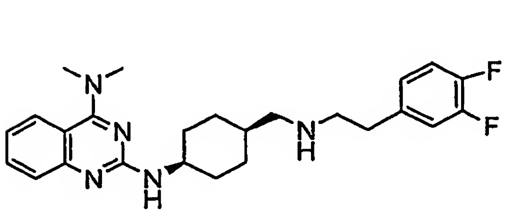
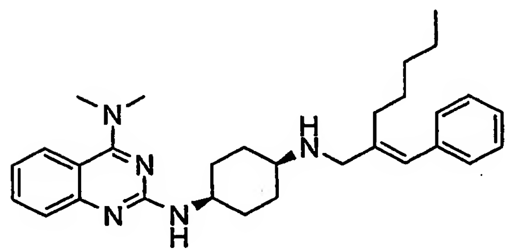
 ,

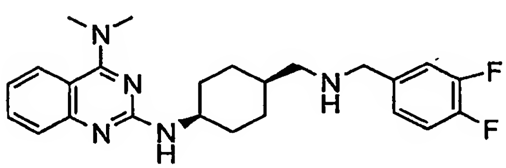
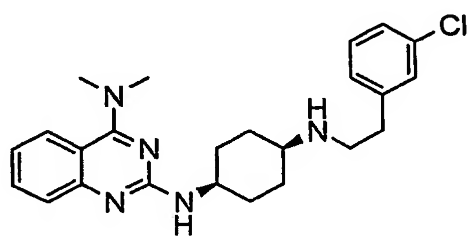
 ,

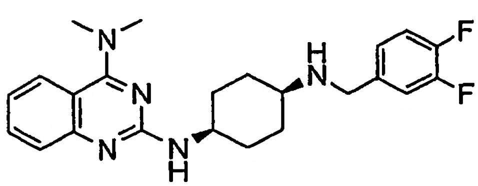
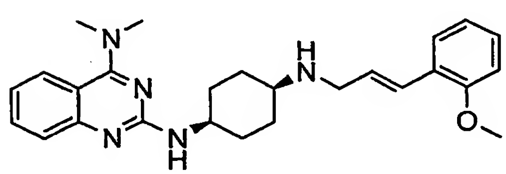

,

,

,

,

,

,

,

,

,

,

,

,

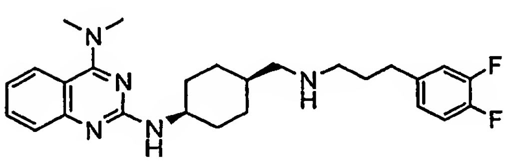
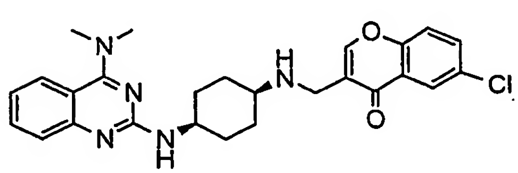
 ,  ,

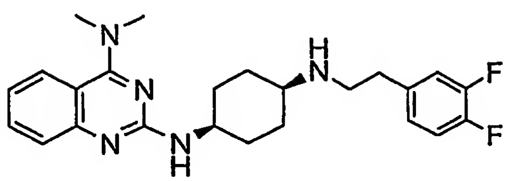
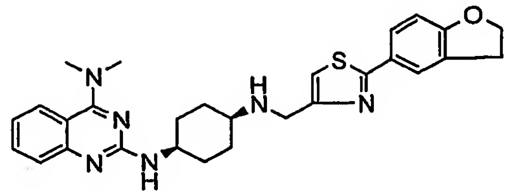
 ,  ,

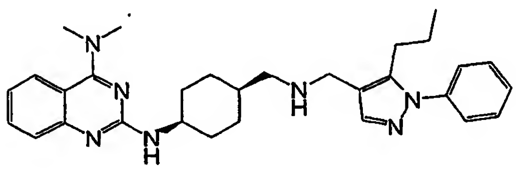
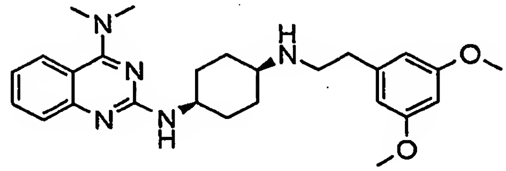
 ,  ,

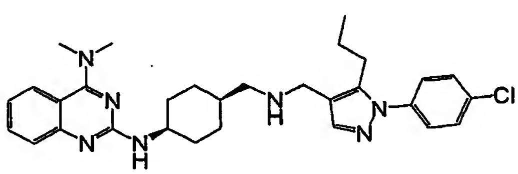
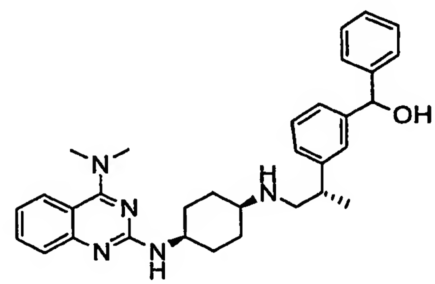
 ,  ,

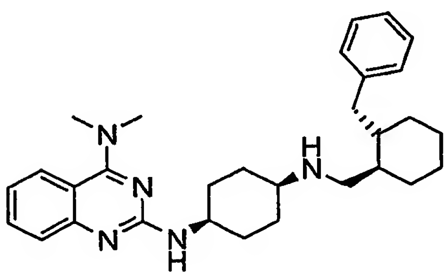
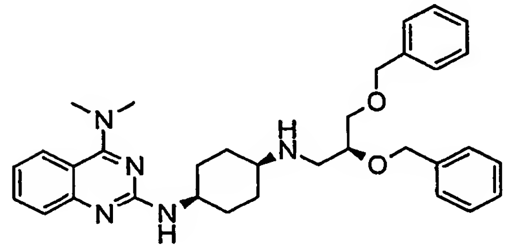
 ,  ,

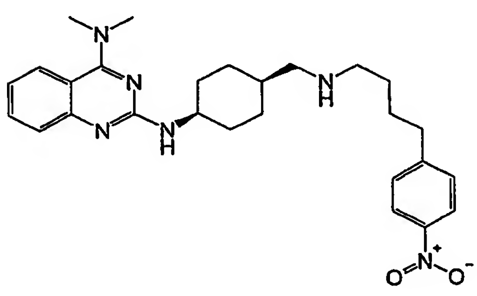
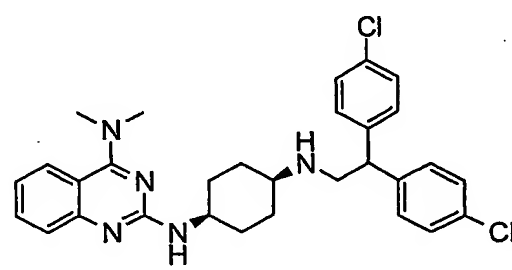
 ,  ,

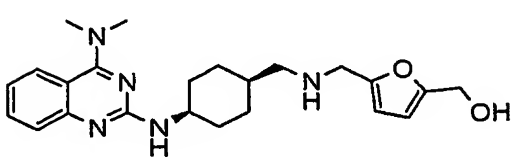
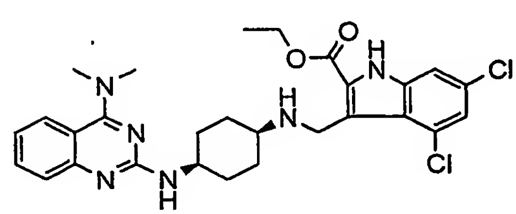

N
N
N
H
H
N
F
F
,

N
N
N
H
H
N
S
N
O
,

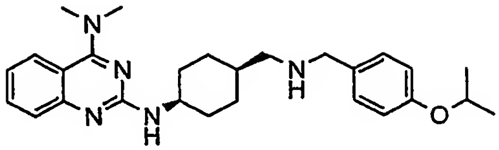
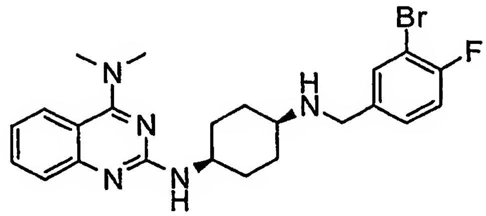
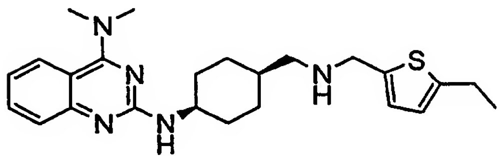
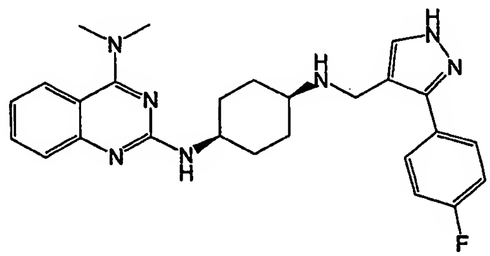
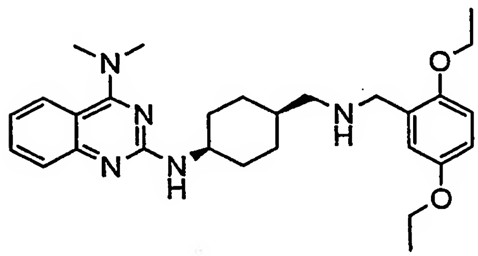
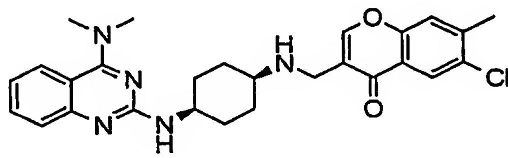
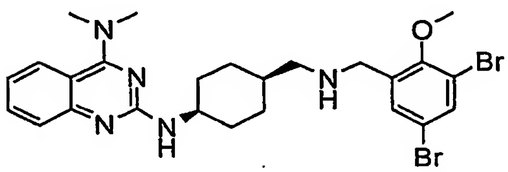
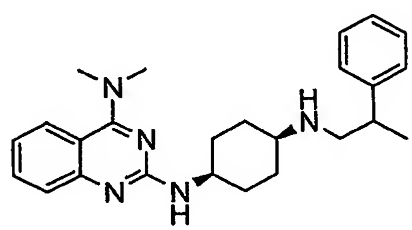
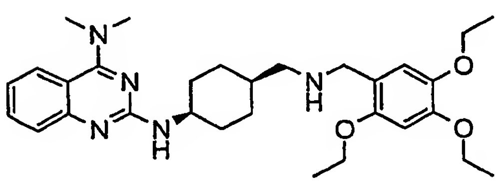
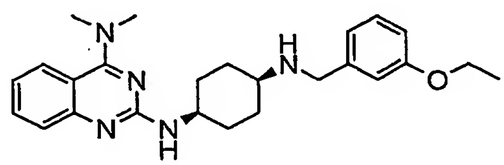
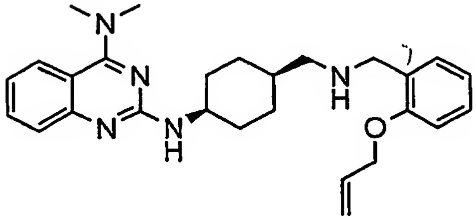
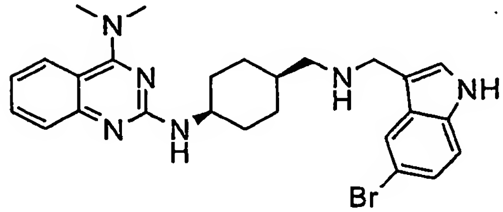

N
N
N
H
N
H
N
N
,

N
N
N
H
H
N
O
O
,

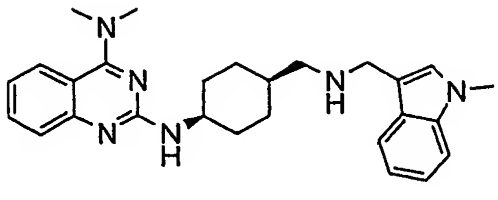
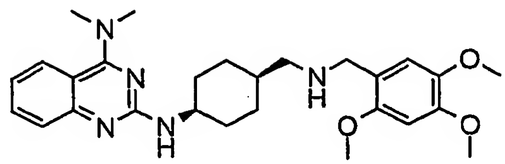

N
N
N
H
N
H
N
N
Cl
,

OH
N
N
N
H
H
N
,

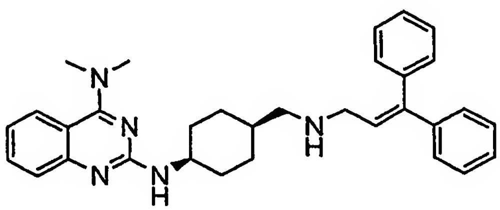
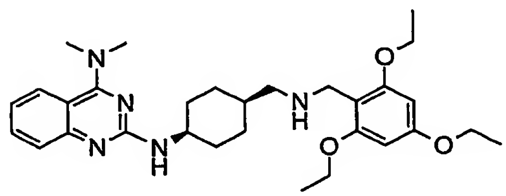

N
N
N
H
H
N
,

N
N
N
H
H
N
O
O
,

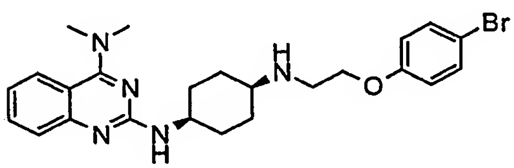
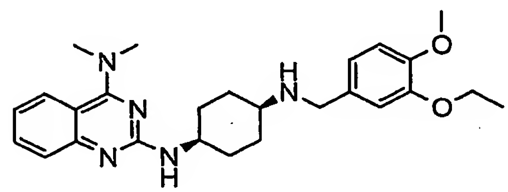

N
N
N
H
N
H
O
N
O
,

Cl
N
N
N
H
H
N
Cl
,

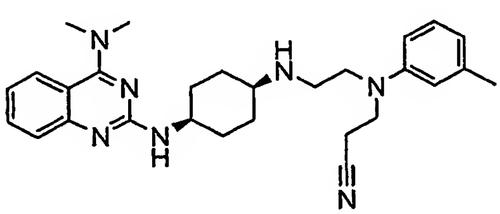
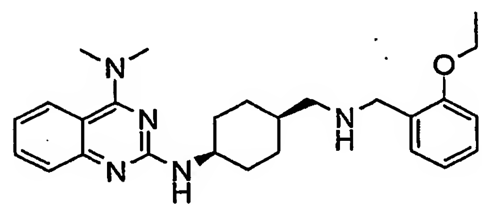

N
N
N
H
N
H
O
OH
,

O
O
H
N
Cl
N
N
N
H
H
N
Cl
,

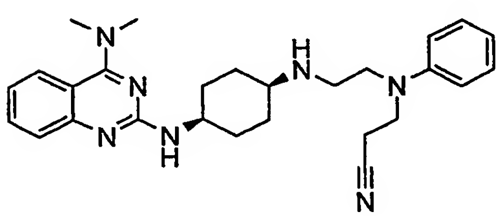
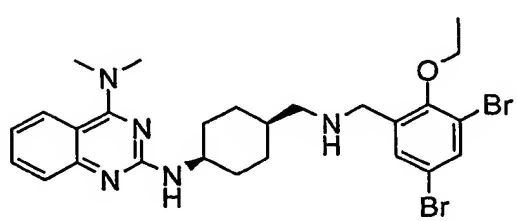

,

,

,

,

,

,

,

,

,

,

,

,

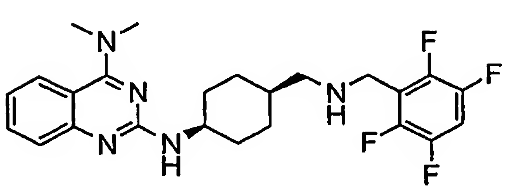
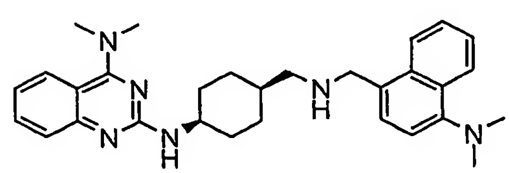
 ,  ,

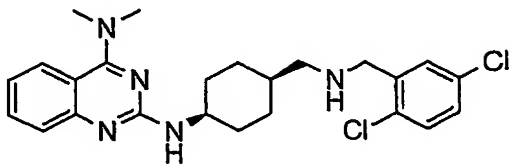
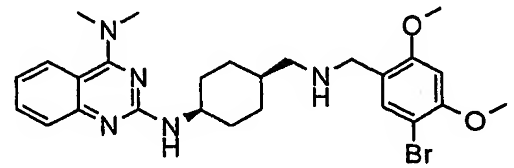
 ,  ,

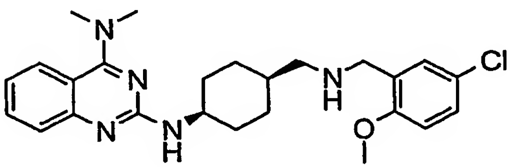
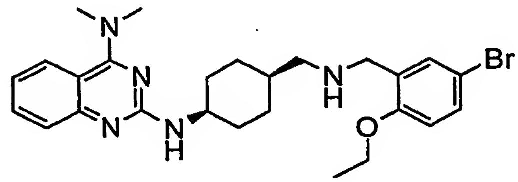
 ,  ,

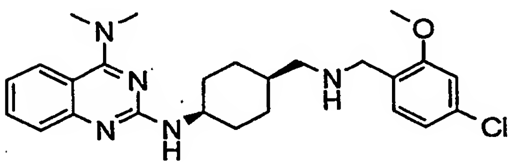
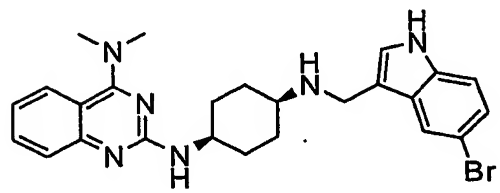
 ,  ,

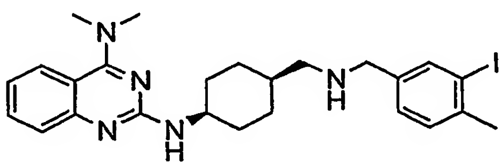
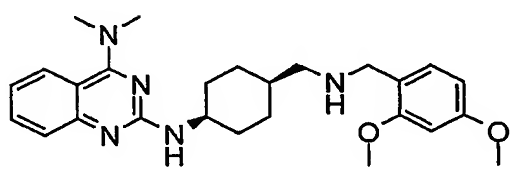
 ,  ,

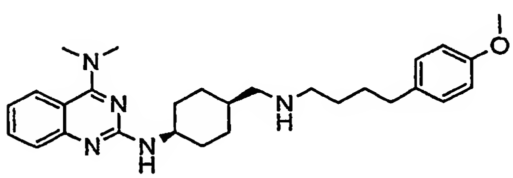
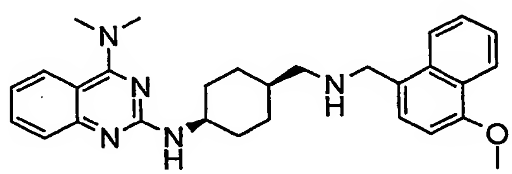
 ,  ,

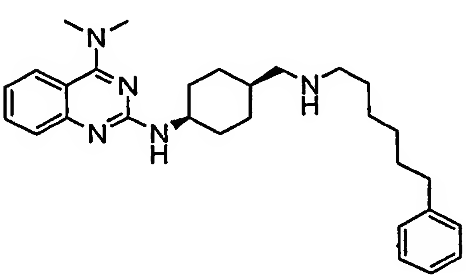
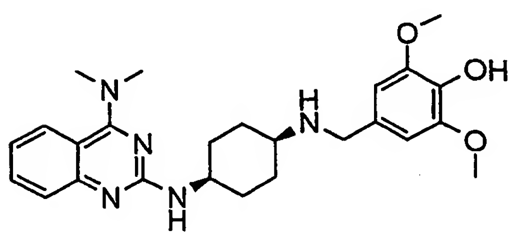
 ,  ,

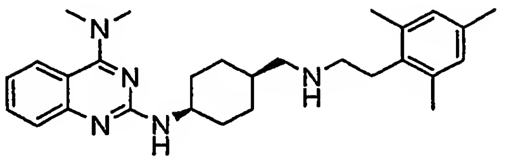
 ,  ,

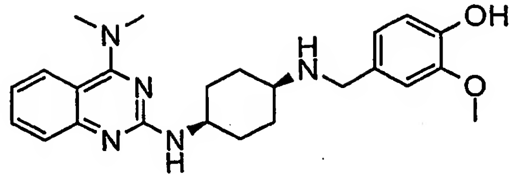
 ,  ,

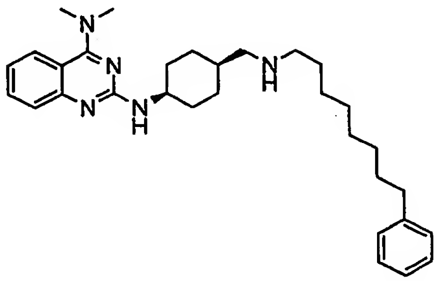
 ,  ,

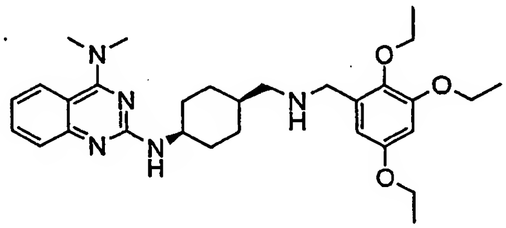
 ,  ,

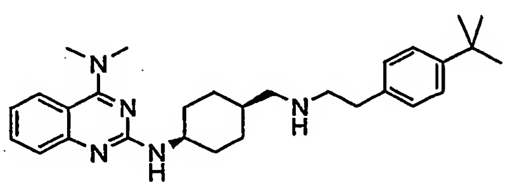
 ,  ,

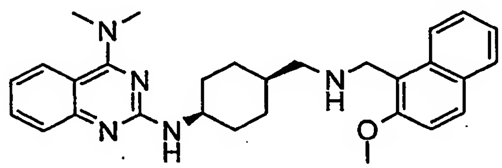
 ,

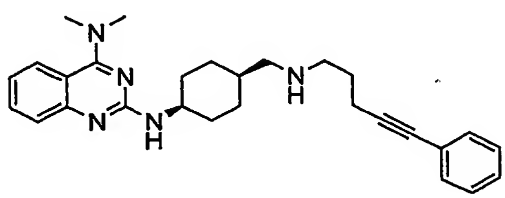
 ,

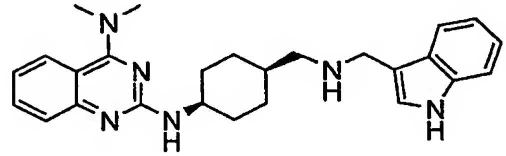
 ,

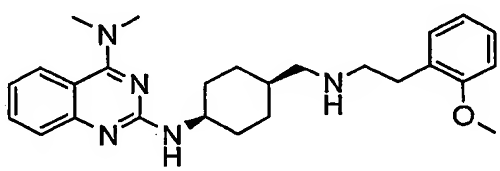
 ,

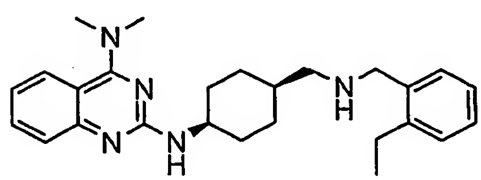
 ,

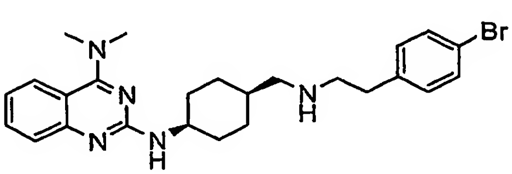
 ,

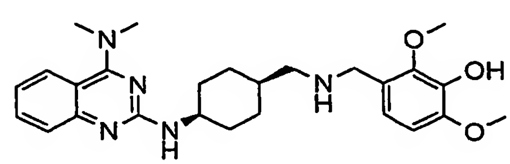
 ,

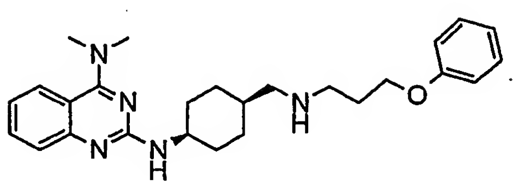
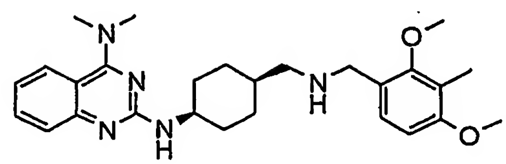
 ,

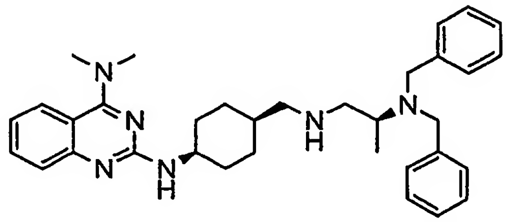
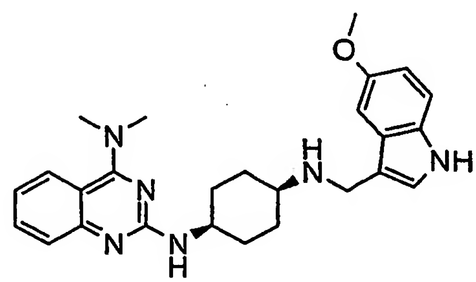
 ,

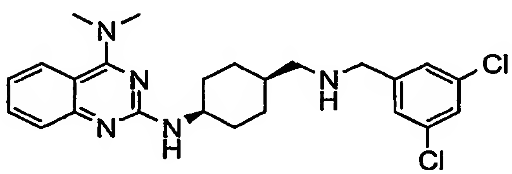
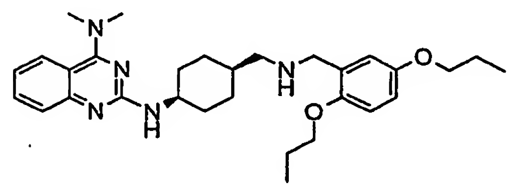
 ,

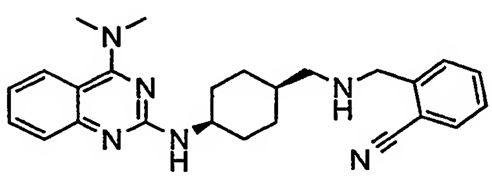
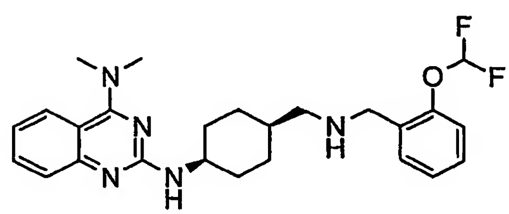
 ,

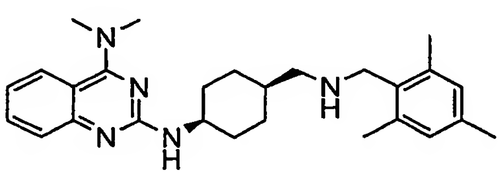
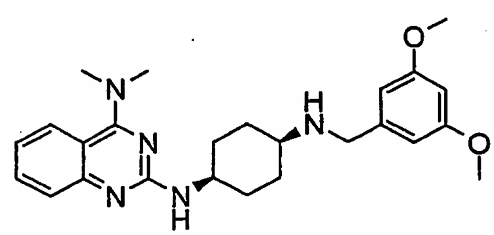
 ,

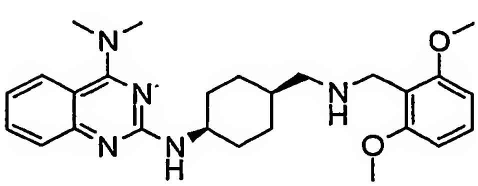
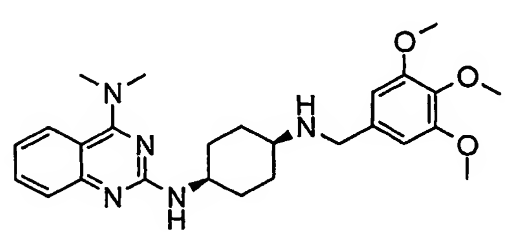
,
,

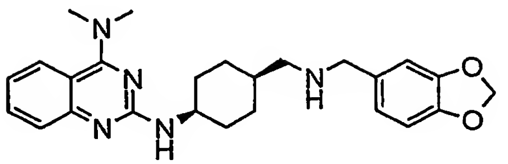
,
,

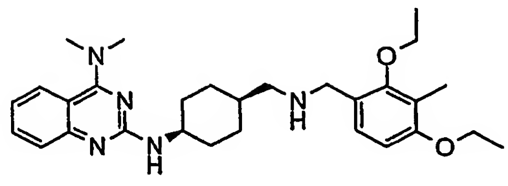
,
,

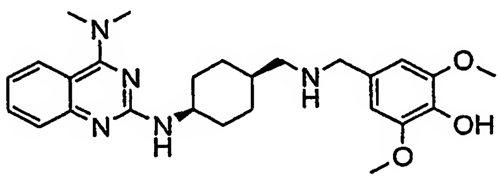
,
,

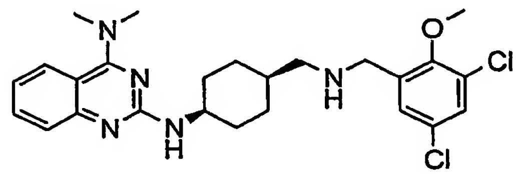
,
,

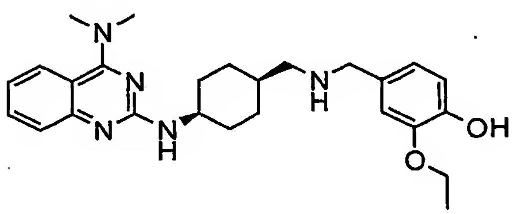
,
,

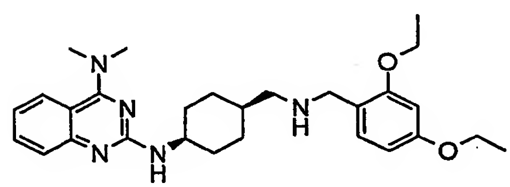
 ,

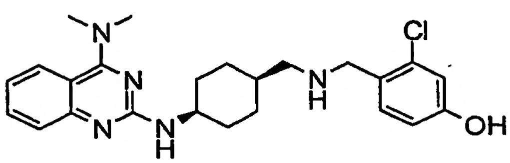
 ,

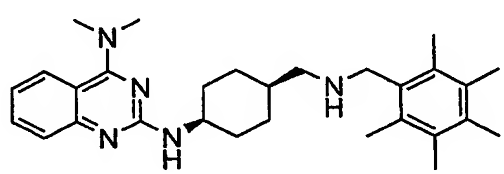
 ,

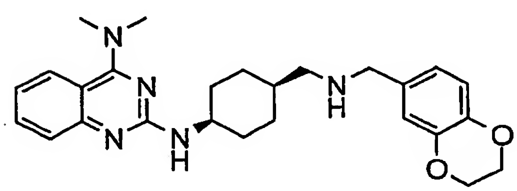
 ,

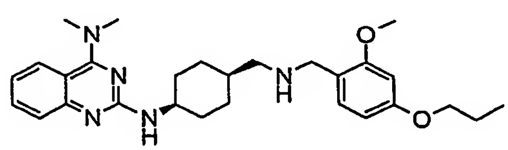
 ,

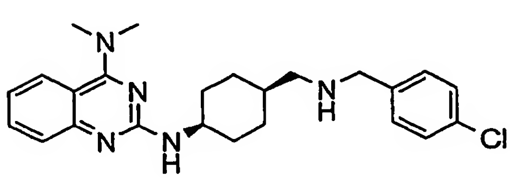
 ,

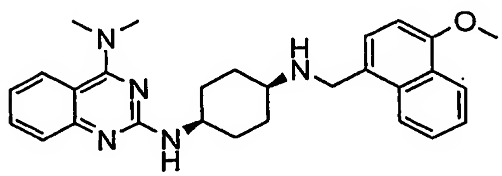
 ,

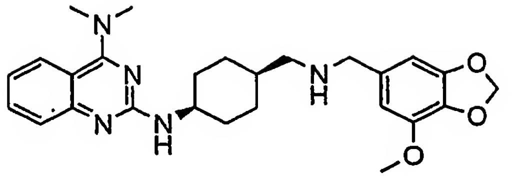
 ,

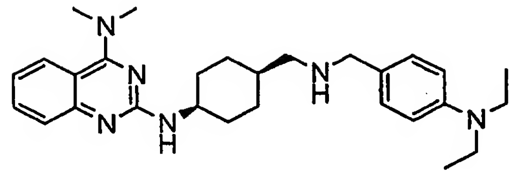
 ,

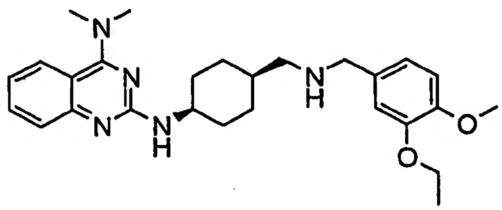
 ,

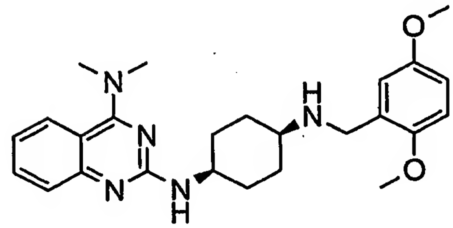
 ,

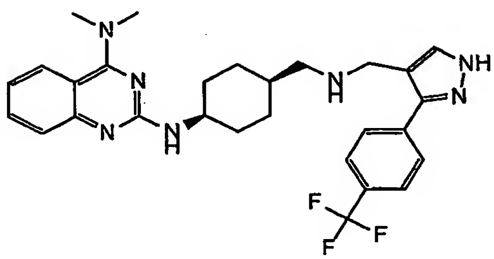
 ,

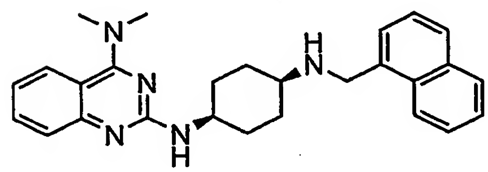
 ,

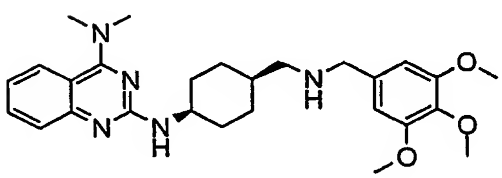
 ,

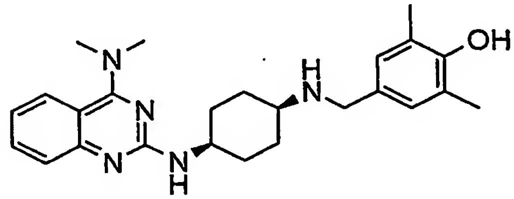
 ,

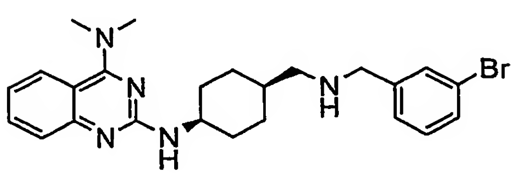
 ,

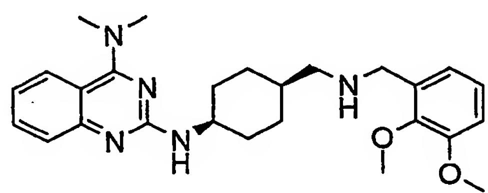
 ,

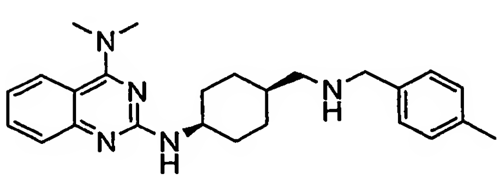
 ,

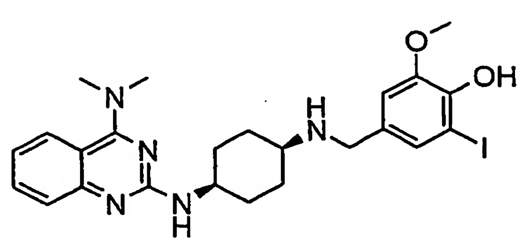
 ,

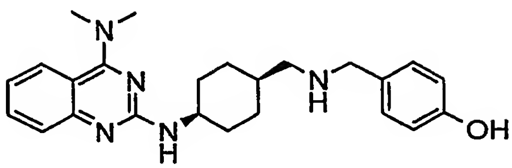
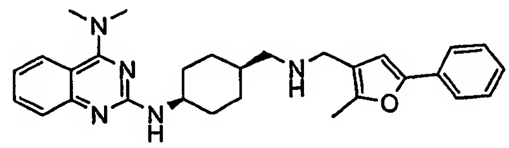
 ;

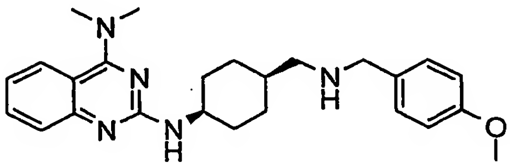
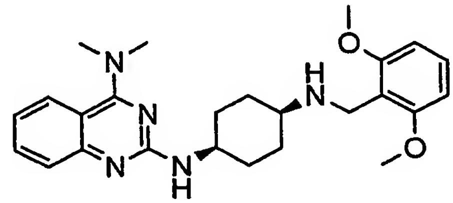
 ,

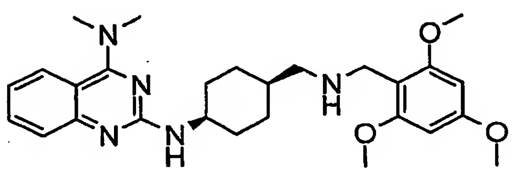
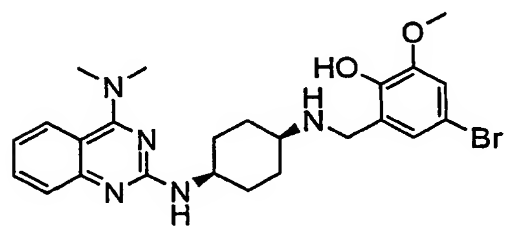
 ,

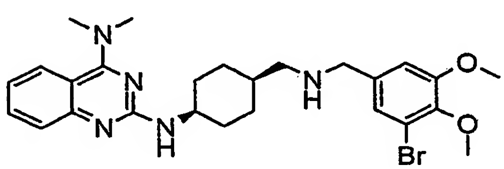
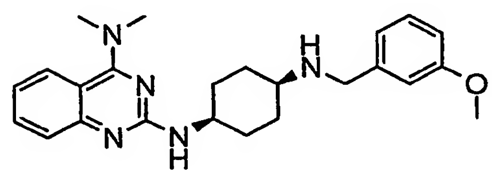
 ,

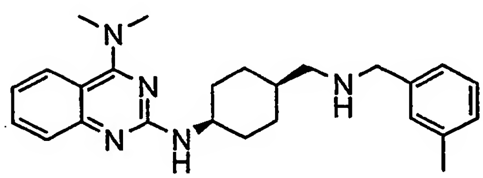
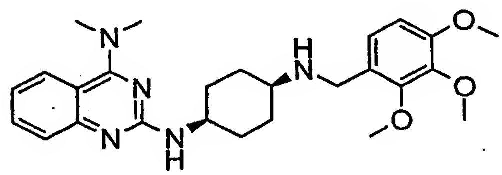
 ,

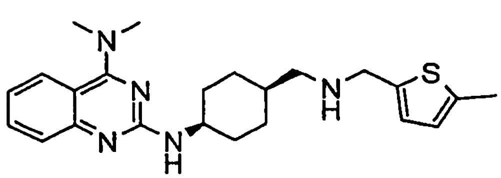
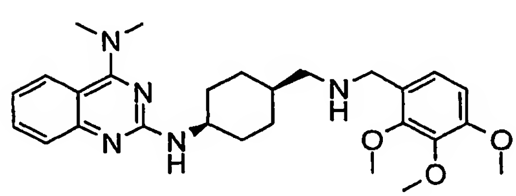
 ,  ,

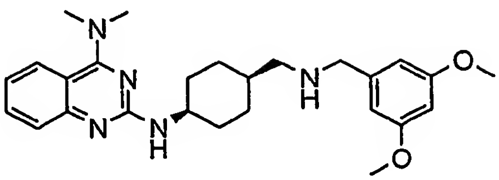
 ,  ,

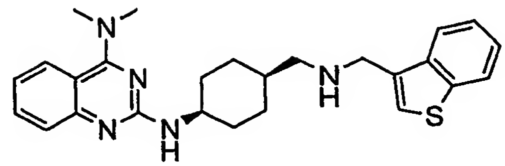
 ,  ,

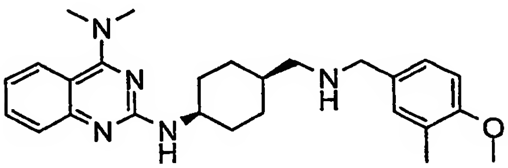
 ,  ,

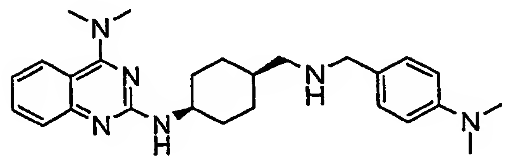
 ,  ,

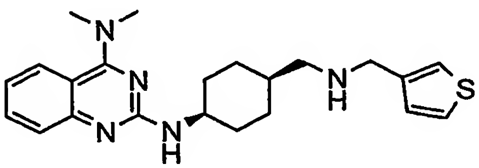
 ,  ,

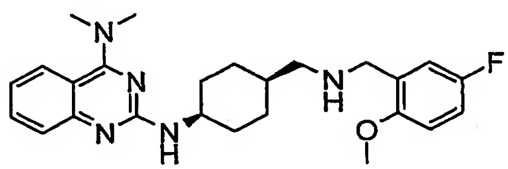
 ,

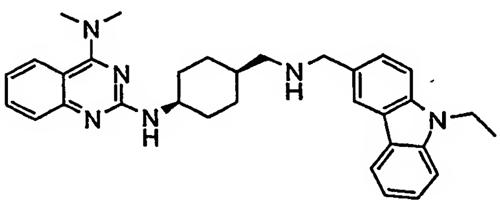
 ,

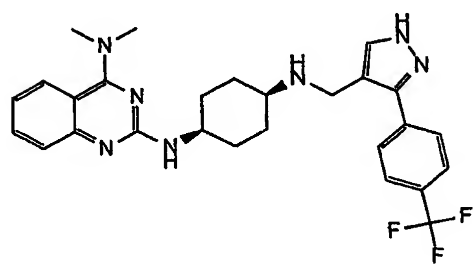
 ,

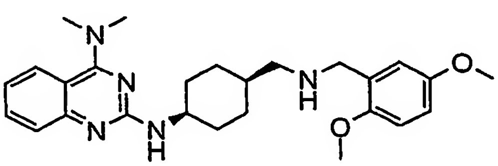
 ,

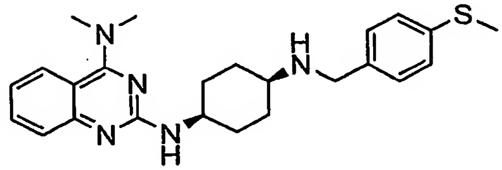
 ,

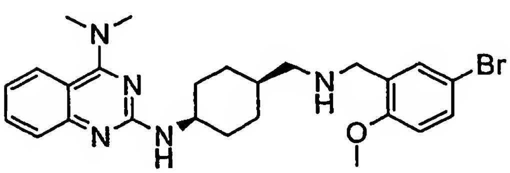
 ,

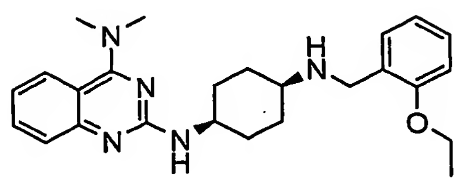
 ,

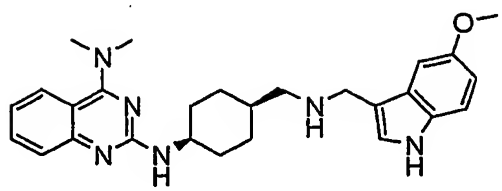
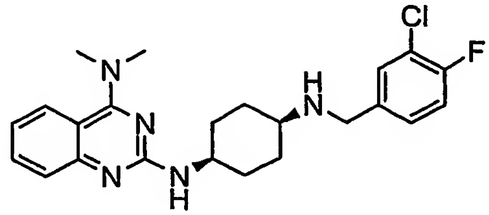
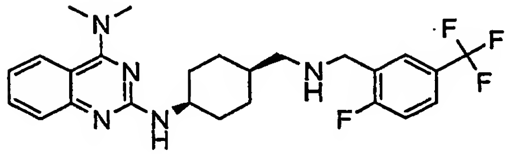
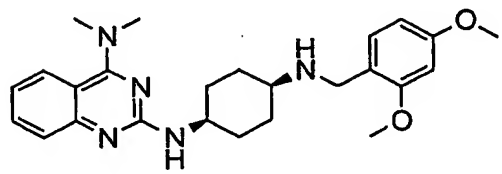
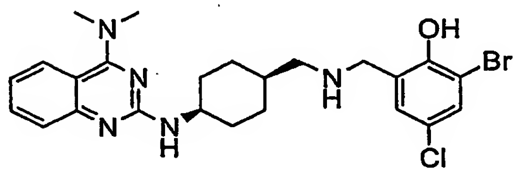
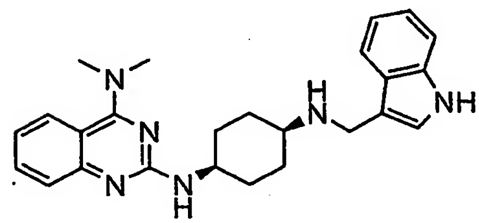
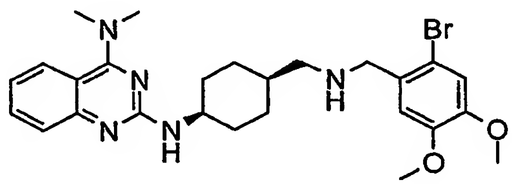
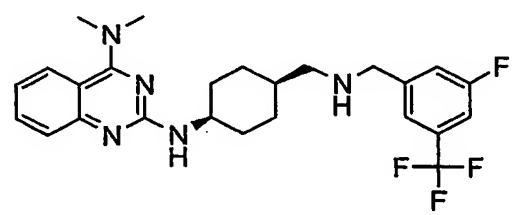
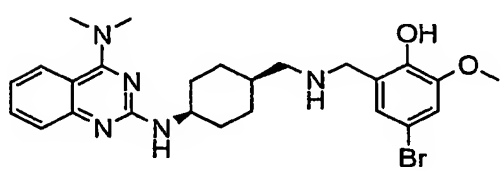
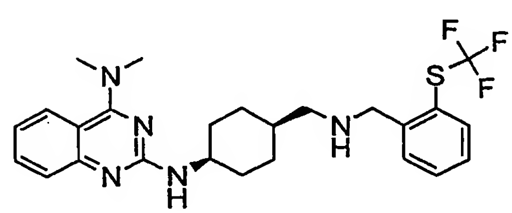
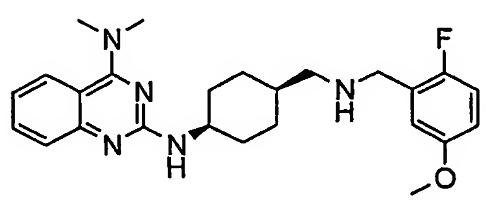
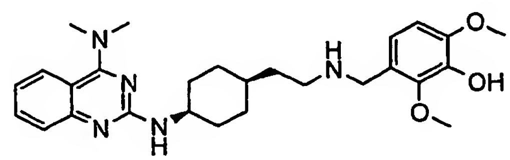
 ,

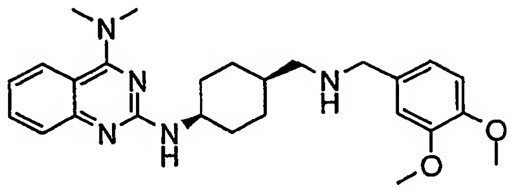
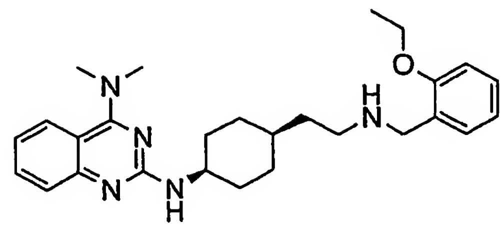
 ,

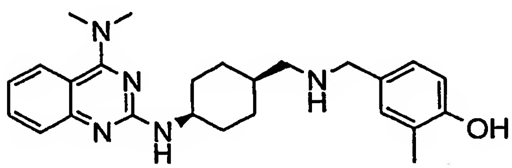
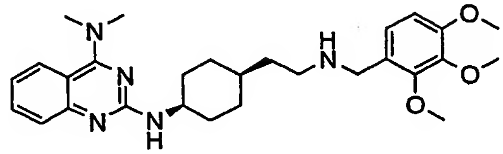
 ,

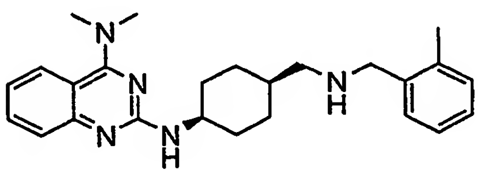
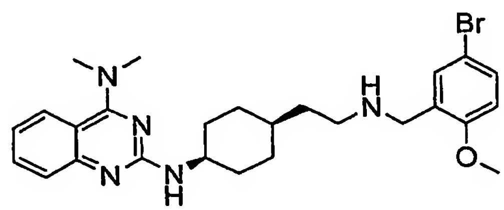
 ,

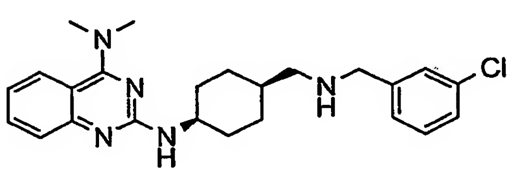
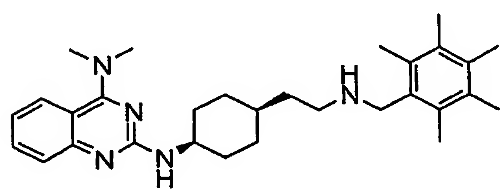
 ,

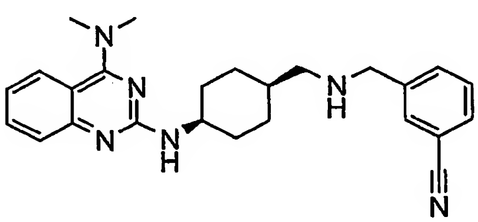
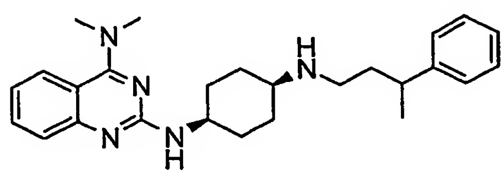

,

,

,

,

,

,

,

;

,

,

,

,

 ,  ,

 ,  ,

 ,  ,

 ,  ,

 , and 

; or, in case of, a salt thereof.

Preferred compounds of this invention are those compounds of Formula I wherein,

Q is Formula II;

R_1 represents

(i) C_1-C_{16} alkyl,

C_1-C_{16} alkyl substituted by substituent(s) independently selected from

•halogen,

•carbocyclyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••nitro,

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl,

(ii) C_2-C_3 alkenyl,

C_2-C_3 alkenyl substituted by carbocyclic aryl,

(iii) carbocyclic aryl,

carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•cyano,

•nitro,

•C_1-C_5 alkyl,

•C_1-C_5 alkyl substituted by substituent(s) independently selected from

••halogen,

••oxo,

•C_2-C_3 alkenyl,

•C_1-C_4 alkoxy,

•C_1-C_4 alkoxy substituted by substituent(s) independently selected from

••halogen,

••heterocyclyl,

••halogenated heterocyclyl,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by substituent(s) independently selected from

••halogen,

••nitro,

•heterocyclyloxy,

•heterocyclyloxy substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl,

•C_1-C_3 alkoxycarbonyl,

•mono- or di-C_1-C_4 alkylamino,

•C_1-C_3 alkylcarbonylamino,

•carbocyclic aryl diazo,

•carbocyclic aryl diazo substituted by mono- or di- C_1-C_3 alkylamino,

•C_1-C_3 alkylsulfonyl,

•carbocyclic aryl,

(iv) heterocyclyl,

or heterocyclyl substituted by substituent(s) independently selected from

•halogen,

•C_1-C_3 alkyl,

• C_1-C_3 alkyl substituted by substituent(s) independently selected from

••halogen,

••oxo,

••carbocyclic arylcarbonylamino,

••halogenated carbocyclic arylcarbonylamino,

••heterocyclyl,

••heterocyclyl substituted by substituent(s) independently selected from

•••halogen,

•••C_1-C_3 alkyl,

•••halogenated C_1-C_3 alkyl,

•C_1-C_3 alkoxy,

•C_1-C_3 alkylcarbonylamino,

•carbocyclic arylsulfonyl,

•C_1-C_3 alkoxycarbonyl,

•carbocyclic aryl,

•halogenated carbocyclic aryl,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl;

R_2 is -$NHNH_2$, -NHNHBoc, -$N(R_{2a})(R_{2b})$, morpholino, 4-acetyl-piperazyl, or 4-phenyl-piperazyl;

wherein R_{2a} is H or C_1-C_3 alkyl;

R_{2b} is C_1-C_4 alkyl, C_1-C_4 alkyl substituted by substituent(s) independently selected from

•hydroxy,

•C_1-C_3 alkoxy,

•amino,

•-NHBoc,

•C_3-C_6 cycloalkyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••-SO_2NH_2,

•heterocyclyl,

C_3-C_6 cycloalkyl, carbocyclic aryl, carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•C_1-C_3 alkyl,

•C_1-C_3 alkoxy,

or a group of Formula IV;

wherein Boc is carbamic acid *tert*-butyl ester and R_3 is C_1-C_3 alkyl or C_1-C_3 alkyl substituted by substituent(s) independently selected from

•carbocyclic aryl,

•halogenated carbocyclic aryl,

•carbocyclic aryl substituted by C_1-C_3 alkoxy;

L is selected from Formula V - XIX;

wherein R_4 is H or C_1-C_3 alkyl;

R_5 is H, C_1-C_3 alkyl, or C_1-C_3 alkyl substituted by a substituted carbocyclic aryl;

Y is -S(O)$_2$-;

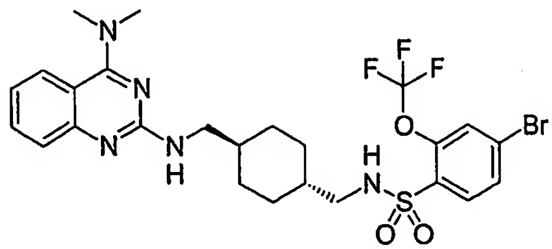
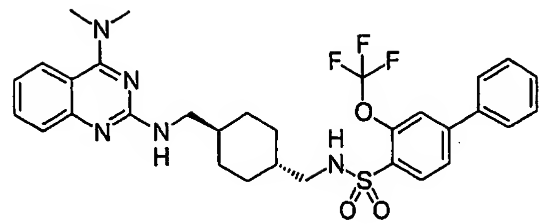
wherein carbocyclic aryl is phenyl, naphthyl, or biphenyl;

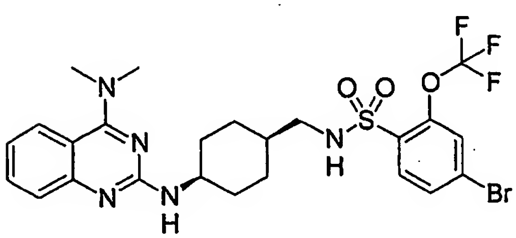
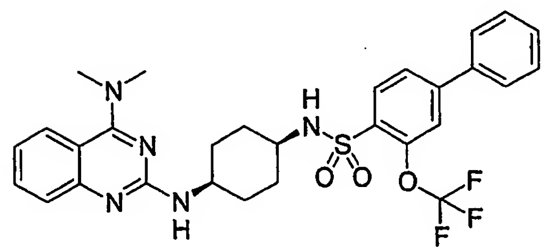
carbocyclyl is 7,7-dimethyl-2-oxo-bicyclo[2.2.1]heptyl;

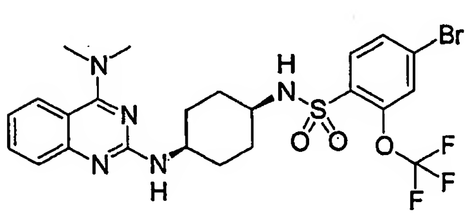
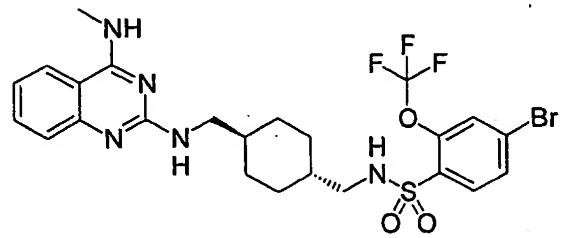
heterocyclyl is 1,2,3,4-tetrahydro-isoquinolyl, 1,2,3-thiadiazolyl, 1*H*-pyrrolyl, benzo[2,1,3]oxadiazolyl, benzo[b]thienyl, furyl, imidazolyl, isoxazolyl, pyrazolyl, pyridyl, quinolyl, thiazolyl, or thienyl;

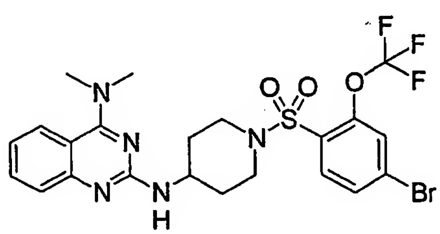
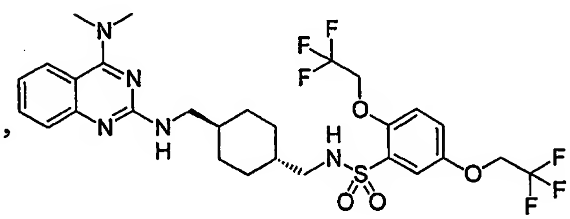
halogen is fluoro, chloro, bromo, or iodo.

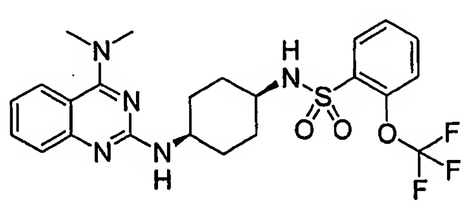
The following compounds are specially preffered;

 ,  ,

 ,  ,

 ,  ,

 ,  ,

and 

; or, in case of, a salt thereof.

Preferred compounds of this invention are those compounds of Formula I wherein,

Q is Fomura II;

R_1 is selected from H, -$CO_2{}^tBu$, or -CO_2Bn (Bn is a benzyl group);

R_2 is methylamino or dimethylamino;

L is selected from Formula XX - XXII;

Y is a single bond;

or a salt thereof.

Also provided in accordance with the present invention are methods of modulating G-protein receptor SLC-1 comprising contacting the SLC-1 receptor with a compound of the invention.

The present invention further provides pharmaceutical compositions containing MCH receptor antagonists of the invention.

Brief Description of the Figures

Figure 1 provides an illustration of IP_3 production from several non-endogenous, constitutively activated version of MCH receptor as compared with the endogenous version of this receptor.

Detailed Description

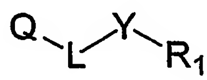
The present invention relates to MCH receptor antagonist compounds, and methods of modulating MCH receptors by contacting the receptors with one or more compounds of the invention.

The term "antagonist" is intended to mean moieties that competitively bind to the receptor at the same site as agonists (for example, the endogenous ligand), but which do not activate the intracellular response initiated by the active form of the receptor, and can thereby inhibit the intracellular responses by agonists or partial agonists. Antagonists do not diminish the baseline intracellular response in the absence of an agonist or partial agonist. As used herein, the term "agonist" is intended to mean moieties that activate the intracellular response when they bind to the receptor, or enhance GTP binding to membranes. In the context of the present invention, a pharmaceutical composition comprising a MCH receptor antagonist of the invention can be utilized for modulating the activity of the MCH receptor,

decreasing body weight and/or affecting metabolism such that the recipient loses weight and/or maintains weight. Such pharmaceutical compositions can be used in the context of disorders and/or diseases where weight gain is a component of the disease and/or disorder such as, for example, obesity.

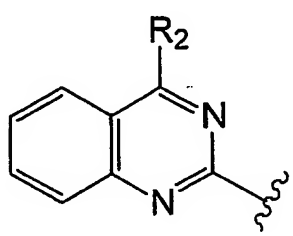
As used herein, the term "contact" or "contacting"shall mean bringing the indicated moieties together, whether in an in vitro system or an in vivo system. Thus, "contacting" an MCH receptor with a compound of the invention includes the administration of a compound of the invention to an animal having an MCH receptor, as well as, for example, introducing a compound of the invention into a sample containing a cellular or more purified preparation containing an MCH receptor.

Compounds of the invention include those having Formula I, shown below:



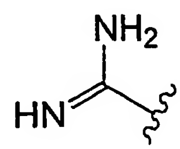
I

wherein Q can be either Foemura II or III: .



II

or



III

R_1 represents

(i) C_1-C_{16} alkyl,

C_1-C_{16} alkyl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•oxo,

•C_1-C_3 alkoxy,

•C_1-C_3 alkoxy substituted by substituent(s) independently selected from

••carbocyclic aryl,

••heterocyclyl,

••heterocyclyl substituted by C_1-C_3 alkyl,

•C_1-C_3 alkylcarbonyloxy,

•carbocyclyloxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by substituent(s) independently selected from

••halogen,

••nitro,

••carbocyclic aryl,

••carbocyclic aryl substituted by C_1-C_3 alkoxy,

••C_1-C_4 alkyl,

••C_1-C_4 alkyl substituted by substituent(s) independently selected from

•••oxo,

•••mono- or di-C_1-C_3 alkylamino,

•••mono- or di-C_1-C_3 alkylamino substituted by carbocyclic aryl,

•••mono- or di-C_1-C_3 alkylamino substituted by halogenated carbocyclic aryl,

•••carbocyclic arylcarbonylamino,

•••halogenated carbocyclic arylcarbonylamino,

•heterocyclyloxy,

•heterocyclyloxy substituted by C_1-C_3 alkyl,

•substituted heterocyclyl-ethylideneaminooxy,

•C_1-C_3 alkoxycarbonyl,

•C_1-C_3 alkoxycarbonyl substituted by carbocyclic aryl,

•mono- or di-C_1-C_3 alkylaminocarbonyl,

•mono- or di-C_1-C_3 alkylamino,

•mono- or di-C_1-C_3 alkylamino substituted by substituent(s) independently selected from

••cyano,

••carbocyclic aryl,

••heterocyclyl,

•mono- or di-carbocyclic arylamino,

•mono- or di-carbocyclic arylamino substituted by substituent(s) independently selected from

••hydroxy,

••C_1-C_3 alkyl,

•C_1-C_3 alkylcalbonylamino,

•C_1-C_3 alkylcalbonylamino substituted by substituent(s) independently selected from

••C_1-C_3 alkylcalbonylamino,

••carbocyclic arylcalbonylamino,

••heterocyclyl,

•C_1-C_4 alkoxycalbonylamino,

•heterocyclyl calbonylamino,

•carbocyclic arylsulfonylamino,

•carbocyclic arylsulfonylamino substituted by substituent(s) independently selected from

••nitro,

••C_1-C_3 alkyl,

••mono- or di-C_1-C_3 alkylamino,

•C_1-C_3 alkylthio,

•C_1-C_3 alkylthio substituted by substituent(s) independently selected from

••mono- or di-carbocyclic arylaminocarbonyl,

••halogenated mono- or di-carbocyclic arylaminocarbonyl,

••mono- or di-carbocyclic arylamino,

••halogenated mono- or di-carbocyclic arylamino,

••carbocyclic aryl,

••carbocyclic aryl substituted by substituent(s) independently selected from

•••halogen,

•••C_1-C_3 alkoxy,

•carbocyclic arylthio,

•carbocyclic arylthio substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

•carbocyclic arylsulfonyl,

•halogenated carbocyclic arylsulfonyl,

•heterocyclylthio,

•heterocyclylthio substituted by substituent(s) independently selected from

••nitro,

••C_1-C_3 alkyl,

•C_3-C_6 cycloalkyl,

•C_3-C_6 cycloalkyl substituted by C_1-C_3 alkyl,

•C_3-C_6 cycloalkenyl,

•carbocyclyl,

•carbocyclyl substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••C_2-C_3 alkenyl,

••C_2-C_3 alkenyl substituted by carbocyclic aryl,

••C_2-C_3 alkenyl substituted by carbocyclic aryl substituted C_1-C_3 alkylsulfinyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••nitro,

••C_1-C_4 alkyl,

••C_1-C_4 alkyl substituted by substituent(s) independently selected from

•••halogen,

•••hydroxy,

•••oxo,

•••carbocyclic aryl,

•••heterocyclyl,

•••mono- or di-carbocyclic arylamino,

•••mono- or di-carbocyclic arylamino substituted by substituent(s) independently selected from

••••halogen,

••••nitro,

••••C_1-C_3 alkyl,

••••C_1-C_3 alkoxy,

••••halogenated C_1-C_3 alkoxy,

••C_1-C_4 alkoxy,

••C_1-C_4 alkoxy substituted by substituent(s) independently selected from

•••halogen,

•••carbocyclic aryl,

••carbocyclic aryloxy,

••C_1-C_3 alkoxycarbonyl,

••C_1-C_3 alkylcarbonyloxy,

••mono- or di-C_1-C_3 alkylamino,

••mono- or di-carbocyclic arylamino,

••halogenated mono- or di-carbocyclic arylamino,

••mono- or di-carbocyclic arylaminocarbonyl,

••mono- or di-carbocyclic arylaminocarbonyl substituted by substituent(s) independently selected from

•••halogen,

•••nitro,

•••C_1-C_3 alkyl,

•••C_1-C_3 alkoxy,

•••halogenated C_1-C_3 alkoxy,

••mercapto,

••C_1-C_3 alkylthio,

••halogenated C_1-C_3 alkylthio,

••C_1-C_3 alkylsulfonyl,

••C_3-C_6 cycloalkyl,

••carbocyclic aryl,

••heterocyclyl,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••hydroxy,

••C_1-C_3 alkyl,

••C_1-C_3 alkyl substituted by carbocyclic aryl,

••C_1-C_3 alkoxy,

••C_1-C_3 alkoxy substituted by carbocyclic aryl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

(ii) C_2-C_8 alkenyl,

C_2-C_8 alkenyl substituted by substituent(s) independently selected from

•halogen,

•oxo,

•C_1-C_3 alkoxy,

•C_1-C_3 alkoxy substituted by carbocyclic aryl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••nitro,

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••halogenated C_1-C_3 alkoxy,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••hydroxy,

••nitro,

••C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

(iii) C_2-C_4 alkynyl,

C_2-C_4 alkynyl substituted by carbocyclic aryl,

(iv) C_3-C_6 cycloalkyl,

C_3-C_6 cycloalkyl substituted by substituent(s) independently selected from

•C_1-C_3 alkyl,

•C_1-C_3 alkyl substituted by substituent(s) independently selected from

••hydroxy,

••oxo,

••carbocyclic aryl,

•mono- or di-C_1-C_3 alkylamino,

•mono- or di-C_1-C_3 alkylamino substituted by carbocyclic aryl,

•carbocyclic arylcarbonylamino,

•carbocyclic aryl,

(v) C_3-C_6 cycloalkeyl,

C_3-C_6 cycloalkeyl substituted by C_1-C_3 alkyl,

(vi) carbocyclyl,

carbocyclyl substituted by substituent(s) independently selected from

•hydroxy,

•nitro,

(vii) carbocyclic aryl,

carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•cyano,

•nitro,

•C_1-C_9 alkyl,

•C_1-C_9 alkyl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••oxo,

••C_1-C_3 alkoxy,

••carbocyclic aryloxy,

••mono- or di-C_1-C_3 alkylamino-N-oxy,

••mono- or di-C_1-C_3 alkylamino,

••mono- or di-C_1-C_3 alkylamino substituted by carbocyclic aryl,

••mono- or di-carbocyclic arylamino,

••carbocyclylimino,

••carbocyclylimino substituted by carbocyclic aryl,

••mono- or di-carbocyclic arylamino,

••mono- or di-carbocyclic arylamino substituted by C_1-C_3 alkoxy,

••mono- or di-carbocyclic arylaminocarbonyl,

••mono- or di-carbocyclic arylaminocarbonyl substituted by C_1-C_3 alkoxy,

••carbocyclic aryl,

••carbocyclic aryl substituted by substituent(s) independently selected from

•••halogen,

•••C_1-C_3 alkyl,

•••halogenated C_1-C_3 alkyl,

••heterocyclyl,

••heterocyclyl substituted by C_1-C_3 alkyl,

•C_2-C_3 alkenyl,

•C_2-C_3 alkenyl substituted by carbocyclic aryl,

•C_1-C_9 alkoxy,

•C_1-C_9 alkoxy substituted by substituent(s) independently selected from

••hydroxy,

••halogen,

••carboxy,

••mono- or di-C_1-C_3 alkylamino,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

••heterocyclyl,

••heterocyclyl substituted by substituent(s) independently selected from

•••halogen,

•••heterocyclyl,

•••heterocyclyl substituted by substituent(s) independently selected from

••••halogen,

••••C_1-C_3 alkyl,

••••halogenated C_1-C_3 alkyl,

•C_2-C_3 alkenyloxy,

•C_1-C_3 alkylcarbonyloxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by substituent(s) independently selected from

••halogen,

••nitro,

••C_1-C_4 alkyl,

••halogenated C_1-C_4 alkyl,

••C_1-C_3 alkoxy,

•heterocyclyloxy,

•heterocyclyloxy substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl,

•(carbocyclic aryl)$S(O)_2O$,

•carboxy,

•C_1-C_3 alkoxycarbonyl,

•mono- or di-C_1-C_3 alkylaminocarbonyl,

•mono- or di-C_1-C_3 alkylaminocarbonyl substituted by carbocyclic aryl,

•mono- or di-carbocyclic arylaminocarbonyl,

•mono- or di-carbocyclic arylaminocarbonyl substituted by C_1-C_3 alkyl,

•amino,

•mono- or di-C_1-C_4 alkylamino,

•mono- or di-C_1-C_4 alkylamino substituted by cyano,

•mono- or di-carbocyclic arylamino,

•C_1-C_3 alkynylcarbonylamino,

•C_1-C_3 alkynylcarbonylamino substituted by carbocyclic aryl,

•carbocyclic arylsulfonylamino,

•carbocyclic arylsulfonylamino substituted by C_1-C_3 alkyl,

•(carbocyclic aryl)NHC(O)NH,

•(carbocyclic aryl)NHC(O)NH substituted by C_1-C_3 alkoxy,

•(carbocyclic aryl)NHC(O)NH substituted by haloganated C_1-C_3 alkoxy,

•carbocyclic aryl diazo,

•carbocyclic aryl diazo substituted by mono- or di- C_1-C_3 alkylamino,

•C_1-C_3 alkylthio,

•halogenated C_1-C_3 alkylthio,

•carbocyclic arylthio,

•carbocyclic arylthio substituted by substituent(s) independently selected from

••halogen,

••cyano,

••C_1-C_3 alkyl,

•heterocyclylthio,

•C_1-C_3 alkylsulfonyl,

•mono- or di-C_1-C_3 alkylaminosulfonyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••C_1-C_7 alkyl,

••halogenated C_1-C_7 alkyl,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••C_1-C_3 alkyl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

(viii) heterocyclyl,

or heterocyclyl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•cyano,

•nitro,

•C_1-C_4 alkyl,

•C_1-C_4 alkyl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••oxo,

••C_1-C_3 alkylcarbonyloxy,

••carbocyclic arylcarbonylamino,

••halogenated carbocyclic arylcarbonylamino,

••C_1-C_3 alkoxycarbonyl,

••C_1-C_3 alkylthio,

••C_1-C_3 alkylthio substituted by carbocyclic aryl,

••C_1-C_3 alkylthio substituted by halogenated carbocyclic aryl,

••carbocyclic aryl,

••carbocyclic aryl substituted by substituent(s) independently selected from

•••halogen,

•••nitro,

••heterocyclyl,

••heterocyclyl substituted by substituent(s) independently selected from

•••halogen,

•••C_1-C_3 alkyl,

•••halogenated C_1-C_3 alkyl,

•C_1-C_3 alkoxy,

•C_1-C_3 alkoxy substituted by carbocyclic aryl,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

•mono- or di-C_1-C_3 alkylamino,

•C_1-C_4 alkylcarbonylamino,

•C_1-C_3 alkylthio,

•C_1-C_3 alkenylthio,

•carbocyclic arylthio,

•halogenated carbocyclic arylthio,

•carbocyclic arylthio substituted by C_1-C_3 alkoxycarbonyl,

•heterocyclylthio,

•heterocyclylthio substituted by C_1-C_3 alkyl,

•C_1-C_3 alkylsulfonyl,

•carbocyclic arylsulfonyl,

•halogenated carbocyclic arylsulfonyl,

•carbocyclic arylsulfonyl substituted by C_1-C_4 alkyl,

•C_1-C_3 alkoxycarbonyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••nitro,

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••halogenated C_1-C_3 alkoxy,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••C_1-C_3 alkoxycarbonyl;

R_2 is -$NHNH_2$, -NHNHBoc, -N(R_{2a})(R_{2b}), morpholino, 4-acetyl-piperazyl, or 4-phenyl-piperazyl;

wherein R_{2a} is H or C_1-C_3 alkyl;

R_{2b} is C_1-C_4 alkyl, C_1-C_4 alkyl substituted by substituent(s) independently selected from

•hydroxy,

•C_1-C_3 alkoxy,

•amino,

•-NHBoc,

•C_3-C_6 cycloalkyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••-SO_2NH_2,

•heterocyclyl,

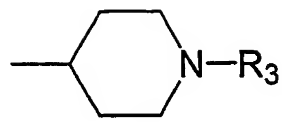
C_3-C_6 cycloalkyl, carbocyclic aryl, carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•C_1-C_3 alkyl,

•C_1-C_3 alkoxy,

or a group of Formula IV;



IV

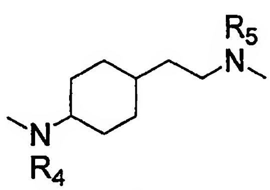
wherein Boc is carbamic acid *tert*-butyl ester and R_3 is C_1-C_3 alkyl or C_1-C_3 alkyl substituted by substituent(s) independently selected from

•carbocyclic aryl,

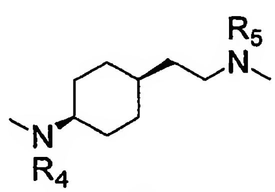
•halogenated carbocyclic aryl,

•carbocyclic aryl substituted by C_1-C_3 alkoxy;

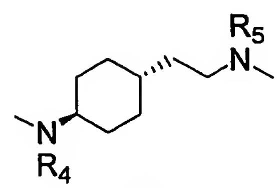
L is selected from Formula V - XIX;



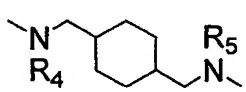
V



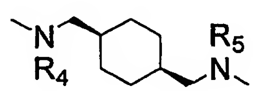
Va



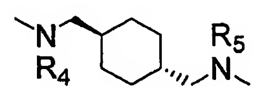
Vb



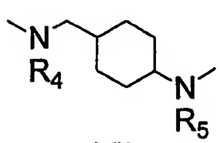
VI



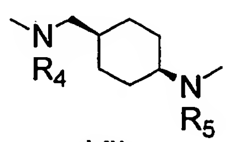
VIa



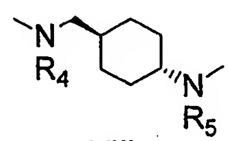
VIb



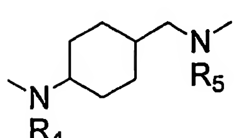
VII



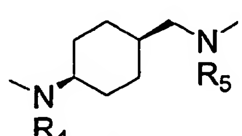
VIIa



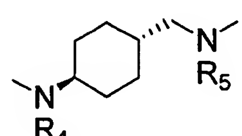
VIIb



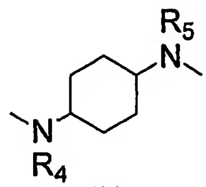
VIII

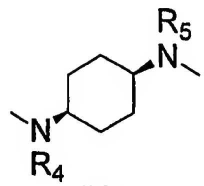


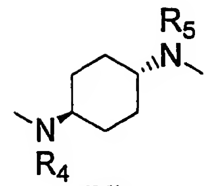
VIIIa

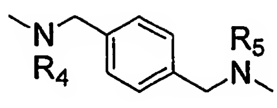


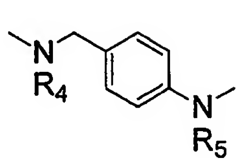
VIIIb

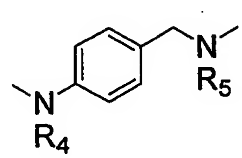

IX

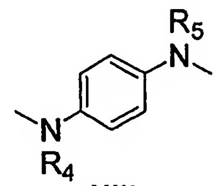

IXa

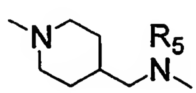

IXb

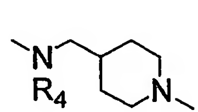

X

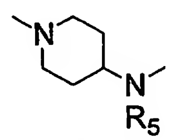

XI

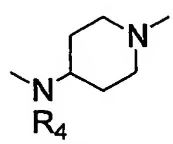

XII

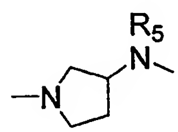

XIII

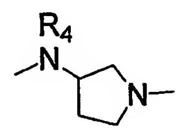

XIV


XV


XVI


XVII


XVIII


XIX

wherein R_4 is H or C_1-C_3 alkyl;

R_5 is H, C_1-C_3 alkyl, or C_1-C_3 alkyl substituted by a substituted carbocyclic aryl;

Y is $-S(O)_2-$, -C(O)-, or $-(CH_2)_m$;

m is 0 or 1;

wherein carbocyclic aryl is phenyl, naphthyl, anthranyl, biphenyl, or phenanthryl;

carbocyclyl is 10,11-dihydro-5-oxo-dibenzo[a,d]cycloheptyl, 1-oxo-indanyl, 7,7-dimethyl-2-oxo-bicyclo[2.2.1]heptyl, 9*H*-fluorenyl, 9-oxo-fluorenyl, acenaphthyl, anthraquinonyl, *C*-fluoren-9-ylidene, indanyl, indenyl, 1,2,3,4-tetrahydro-naphthyl, or bicyclo[2.2.1]hepteny;

heterocyclyl is 1,2,3,4-tetrahydro-isoquinolyl, 1,2,3-thiadiazolyl, 1,2,3-triazolyl,

1,2-dihydro-3-oxo-pyrazolyl, 1,3,4-thiadiazolyl, 1,3-dioxo-isoindolyl, 1,3-dioxolanyl, 1*H*-indolyl, 1*H*-pyrrolo[2,3-c]pyridyl, 1*H*-pyrrolyl, 1-oxo-3*H*-isobenzofuranyl, 2,2',5',2"-terthiophenyl, 2,2'-bithiophenyl, 2,3-dihydro-1-oxo-isoindolyl, 2,3-dihydro-benzo[1,4]dioxinyl, 2,3-dihydro-benzofuryl, 2,4-dihydro-3-oxo-pyrazolyl, 2*H*-benzopyranyl, 2-oxo-benzopyranyl, 2-oxo-pyrrolidinyl, 3,4-dihydro-2*H*-benzo[1,4]oxazinyl, 3,4-dihydro-2*H*-benzo[b][1,4]dioxepinyl, 4*H*-benzo[1,3]dioxinyl, 4*H*-benzopyranyl, 4-oxo-1,5,6,7-tetrahydro-indolyl, 4-oxo-3,4-dihydro-phthalazinyl, 4-oxo-benzopyranyl, 9,10,10-trioxo-thioxanthenyl, 9*H*-carbazolyl, 9*H*-xanthenyl, azetidinyl, benzimidazolyl, benzo[1,3]dioxolyl, benzo[2,1,3]oxadiazolyl, benzo[b]thienyl, benzofuryl, benzothiazolyl, cinnolyl, furyl, imidazo[2,1-b]thiazolyl, imidazolyl, isoxazolyl, morpholino, morpholinyl, oxazolyl, oxolanyl, piperazyl, piperidyl, piridyl, pyrazolo[5,1-b]thiazolyl, pyrazolyl, pyridyl, pyrimidyl, pyrrolidyl, quinolyl, quinoxalyl, thiazolidyl, thiazolyl, thienyl, thiolanyl, 2,3-dihydro-benzofuryl, tetrahydro-thienyl, or benzofuranyl;

halogen is fluoro, chloro, bromo, or iodo.

Preferred compounds of this invention are those compounds of Formula I wherein,

Q is Formula II;

R_1 represents

(i) C_1-C_{10} alkyl,

C_1-C_{10} alkyl substituted by substituent(s) independently selected from

•halogen,

•oxo,

•C_1-C_3 alkoxy,

•C_1-C_3 alkoxy substituted by carbocyclic aryl,

•C_1-C_3 alkylcarbonyloxy,

•carbocyclyloxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by substituent(s) independently selected from

••halogen,

••nitro,

••C_1-C_4 alkyl,

••C_1-C_4 alkyl substituted by substituent(s) independently selected from

•••oxo,

•••carbocyclic arylcarbonylamino,

•••halogenated carbocyclic arylcarbonylamino,

•heterocyclyloxy,

•heterocyclyloxy substituted by C_1-C_3 alkyl,

•substituted heterocyclyl-ethylideneaminooxy,

•C_1-C_3 alkoxycarbonyl,

•C_1-C_3 alkoxycarbonyl substituted by carbocyclic aryl,

•mono- or di-C_1-C_3 alkylaminocarbonyl,

•mono- or di-carbocyclic arylamino,

•mono- or di-carbocyclic arylamino substituted by hydroxy,

•C_1-C_3 alkylcalbonylamino,

•C_1-C_3 alkylcalbonylamino substituted by substituent(s) independently selected from

••C_1-C_3 alkylcalbonylamino,

••carbocyclic arylcalbonylamino,

••heterocyclyl,

•C_1-C_4 alkoxycalbonylamino,

•heterocyclyl calbonylamino,

•carbocyclic arylsulfonylamino,

•carbocyclic arylsulfonylamino substituted by substituent(s) independently selected from

••nitro,

••C_1-C_3 alkyl,

••mono- or di-C_1-C_3 alkylamino,

•C_1-C_3 alkylthio,

•C_1-C_3 alkylthio substituted by substituent(s) independently selected from

••mono- or di-carbocyclic arylaminocarbonyl,

••halogenated mono- or di-carbocyclic arylaminocarbonyl,

••carbocyclic aryl,

••carbocyclic aryl substituted by substituent(s) independently selected from

•••halogen,

•••C_1-C_3 alkoxy,.

•carbocyclic arylthio,

•carbocyclic arylthio substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

•carbocyclic arylsulfonyl,

•halogenated carbocyclic arylsulfonyl,

•heterocyclylthio,

•heterocyclylthio substituted by substituent(s) independently selected from

••nitro,

••C_1-C_3 alkyl,

•C_3-C_6 cycloalkyl,

•C_3-C_6 cycloalkyl substituted by C_1-C_3 alkyl,

•C_3-C_6 cycloalkenyl,

•carbocyclyl,

•carbocyclyl substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••C_2-C_3 alkenyl,

••C_2-C_3 alkenyl substituted by carbocyclic aryl,

••C_2-C_3 alkenyl substituted by carbocyclic aryl substituted C_1-C_3 alkylsulfinyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••nitro,

••C_1-C_4 alkyl,

••C_1-C_4 alkyl substituted by substituent(s) independently selected from

•••oxo,

•••carbocyclic aryl,

•••heterocyclyl,

••C_1-C_4 alkoxy,

••C_1-C_4 alkoxy substituted by substituent(s) independently selected from

•••halogen,

•••carbocyclic aryl,

••carbocyclic aryloxy,

••C_1-C_3 alkylcarbonyloxy,

••mono- or di-carbocyclic arylamino,

••halogenated mono- or di-carbocyclic arylamino,

••mono- or di-carbocyclic arylaminocarbonyl,

••mono- or di-carbocyclic arylaminocarbonyl substituted by substituent(s) independently selected from

•••halogen,

•••nitro,

•••C_1-C_3 alkyl,

•••C_1-C_3 alkoxy,

•••halogenated C_1-C_3 alkoxy,

••mercapto,

••C_1-C_3 alkylthio,

••halogenated C_1-C_3 alkylthio,

••C_1-C_3 alkylsulfonyl,

••C_3-C_6 cycloalkyl,

••carbocyclic aryl,

••heterocyclyl,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••hydroxy,

••C_1-C_3 alkyl,

••C_1-C_3 alkyl substituted by carbocyclic aryl,

••C_1-C_3 alkoxy,

••C_1-C_3 alkoxy substituted by carbocyclic aryl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

(ii) C_2-C_6 alkenyl,

C_2-C_6 alkenyl substituted by substituent(s) independently selected from

•oxo,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••nitro,

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••halogenated C_1-C_3 alkoxy,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••hydroxy,

••C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

(iii) C_3-C_6 cycloalkyl,

C_3-C_6 cycloalkyl substituted by substituent(s) independently selected from

•C_1-C_3 alkyl,

•C_1-C_3 alkyl substituted by substituent(s) independently selected from

••oxo,

••carbocyclic aryl,

•carbocyclic arylcarbonylamino,

•carbocyclic aryl,

(iv) carbocyclyl,

carbocyclyl substituted by nitro,

(v) carbocyclic aryl,

carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•cyano,

•nitro,

•C_1-C_9 alkyl,

•C_1-C_9 alkyl substituted by substituent(s) independently selected from

••halogen,

••oxo,

••carbocyclic aryloxy,

••carbocyclylimino,

••carbocyclylimino substituted by carbocyclic aryl,

••mono- or di-carbocyclic arylaminocarbonyl,

••mono- or di-carbocyclic arylaminocarbonyl substituted by C_1-C_3 alkoxy,

••carbocyclic aryl,

••carbocyclic aryl substituted by substituent(s) independently selected from

•••halogen,

•••C_1-C_3 alkyl,

•••halogenated C_1-C_3 alkyl,

••heterocyclyl,

••heterocyclyl substituted by C_1-C_3 alkyl,

•C_1-C_7 alkoxy,

•C_1-C_7 alkoxy substituted by substituent(s) independently selected from

••halogen,

••carbocyclic aryl,

•C_1-C_3 alkylcarbonyloxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by C_1-C_3 alkoxy,

•C_1-C_3 alkoxycarbonyl,

•mono- or di-C_1-C_3 alkylaminocarbonyl,

•mono- or di-C_1-C_3 alkylaminocarbonyl substituted by carbocyclic aryl,

•mono- or di-carbocyclic arylaminocarbonyl,

•mono- or di-carbocyclic arylaminocarbonyl substituted by C_1-C_3 alkyl,

•amino,

•mono- or di-C_1-C_3 alkylamino,

•C_1-C_3 alkynylcarbonylamino,

•C_1-C_3 alkynylcarbonylamino substituted by carbocyclic aryl,

•carbocyclic arylsulfonylamino,

•carbocyclic arylsulfonylamino substituted by C_1-C_3 alkyl,

•(carbocyclic aryl)NHC(O)NH,

•(carbocyclic aryl)NHC(O)NH substituted by C_1-C_3 alkoxy,

•(carbocyclic aryl)NHC(O)NH substituted by haloganated C_1-C_3 alkoxy,

•C_1-C_3 alkylthio,

•halogenated C_1-C_3 alkylthio,

•carbocyclic arylthio,

•carbocyclic arylthio substituted by cyano,

•C_1-C_3 alkylsulfonyl,

•mono- or di-C_1-C_3 alkylaminosulfonyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••C_1-C_7 alkyl,

••halogenated C_1-C_7 alkyl,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••C_1-C_3 alkyl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

(vi) heterocyclyl,

or heterocyclyl substituted by substituent(s) independently selected from

•halogen,

•nitro,

•C_1-C_4 alkyl,

•C_1-C_4 alkyl substituted by substituent(s) independently selected from

••halogen,

••oxo,

••C_1-C_3 alkylthio,

••C_1-C_3 alkylthio substituted by carbocyclic aryl,

••C_1-C_3 alkylthio substituted by halogenated carbocyclic aryl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

••heterocyclyl,

•C_1-C_3 alkoxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

•C_1-C_3 alkylthio,

•C_1-C_3 alkenylthio,

•carbocyclic arylthio,

•C_1-C_3 alkylsulfonyl,

•carbocyclic arylsulfonyl,

•halogenated carbocyclic arylsulfonyl,

•carbocyclic arylsulfonyl substituted by C_1-C_4 alkyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••nitro,

••C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl;

R_2 is -$NHNH_2$, -NHNHBoc, -N(R_{2a})(R_{2b}), morpholino, 4-acetyl-piperazyl, or 4-phenyl-piperazyl;

wherein R_{2a} is H or C_1-C_3 alkyl;

R_{2b} is C_1-C_4 alkyl, C_1-C_4 alkyl substituted by substituent(s) independently selected from

•hydroxy,

•C_1-C_3 alkoxy,

•amino,

•-NHBoc,

•C_3-C_6 cycloalkyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••-SO_2NH_2,

•heterocyclyl,

C_3-C_6 cycloalkyl, carbocyclic aryl, carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•C_1-C_3 alkyl,

•C_1-C_3 alkoxy,

or a group of Formula IV;

wherein Boc is carbamic acid *tert*-butyl ester and R_3 is C_1-C_3 alkyl or C_1-C_3 alkyl substituted by substituent(s) independently selected from

•carbocyclic aryl,

•halogenated carbocyclic aryl,

•carbocyclic aryl substituted by C_1-C_3 alkoxy;

L is selected from Formula V - XIX;

wherein R_4 is H or C_1-C_3 alkyl;

R_5 is H, C_1-C_3 alkyl, or C_1-C_3 alkyl substituted by a substituted carbocyclic aryl;

Y is -C(O)-;

wherein carbocyclic aryl is phenyl, naphthyl, anthranyl, or biphenyl;

carbocyclyl is 10,11-dihydro-5-oxo-dibenzo[a,d]cycloheptyl, 1-oxo-indanyl, 9*H*-fluorenyl, 9-oxo-fluorenyl, acenaphthyl, anthraquinonyl, *C*-fluoren-9-ylidene, indanyl, indenyl, 1,2,3,4-tetrahydro-naphthyl, or bicyclo[2.2.1]hepteny;

heterocyclyl is 1,2,3-thiadiazolyl, 1,2,3-triazolyl, 1,2-dihydro-3-oxo-pyrazolyl, 1,3-dioxo-isoindolyl, 1*H*-indolyl, 1*H*-pyrrolyl, 1-oxo-3*H*-isobenzofuranyl, 2,3-dihydro-benzo[1,4]dioxinyl, 2,3-dihydro-benzofuryl, 2,4-dihydro-3-oxo-pyrazolyl, 2*H*-benzopyranyl, 2-oxo-benzopyranyl, 2-oxo-pyrrolidinyl, 3,4-dihydro-2*H*-benzo[b][1,4]dioxepinyl, 4-oxo-1,5,6,7-tetrahydro-indolyl, 4-oxo-3,4-dihydro-phthalazinyl, 4-oxo-benzopyranyl, 9,10,10-trioxo-thioxanthenyl, 9*H*-xanthenyl, azetidinyl, benzimidazolyl, benzo[1,3]dioxolyl, benzo[2,1,3]oxadiazolyl, benzo[b]thienyl, cinnolyl,

furyl, imidazolyl, isoxazolyl, morpholino, morpholinyl, oxazolyl, oxolanyl, piperidyl, piridyl, pyrazolyl, pyridyl, pyrimidyl, pyrrolidyl, quinolyl, quinoxalyl, thiazolidyl, thiazolyl, thienyl, thiolanyl, tetrahydro-thienyl, benzofuranyl, or benzothiazolyl;

halogen is fluoro, chloro, bromo, or iodo.

Other preferred compounds of this invention are those compounds of Formula I wherein,

Q is Formula II;

R_1 represents

(i) C_1-C_{10} alkyl,

C_1-C_{10} alkyl substituted by substituent(s) independently selected from

•oxo,

•di-propylaminocarbonyl,

•methoxy substituted by carbocyclic aryl,

•methylcarbonyloxy,

•carbocyclic aryloxy,

•halogenated carbocyclic aryloxy,

•carbocyclic aryloxy substituted by nitro,

•heterocyclyloxy substituted by methyl,

•substituted heterocyclyl-ethylideneaminooxy,

•*tert*-butoxycarbonylamino,

•carbocyclic arylcarbonylamino,

•C_1-C_2 alkylthio,

•C_1-C_2 alkylthio substituted by substituent(s) independently selected from

••halogenated carbocyclic aryl,

••carbocyclic aryl substituted by methoxy,

•carbocyclic arylthio,

•hetrocyclylthio substituted by nitro,

•hetrocyclylthio substituted by methyl,

•C_5-C_6 cycloalkyl,

•C_5-C_6 cycloalkenyl,

•carbocyclyl substituted by substituent(s) independently selected from

••halogen,

••methyl,

••methoxy,

••ethenyl substituted by carbocyclic aryl substituted methylsulfinyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••nitro,

••C_1-C_4 alkyl,

••C_1-C_4 alkyl substituted by substituent(s) independently selected from

•••oxo,

•••carbocyclic aryl,

•••heterocyclyl,

••C_1-C_4 alkoxy,

••halogenated C_1-C_4 alkoxy,

••C_1-C_4 alkoxy substituted by carbocyclic aryl,

••carbocyclic aryloxy,

••halogenated mono-carbocyclic arylaminocarbonyl,

••carbocyclic aryl,

••heterocyclyl,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••C_1-C_2 alkyl,

•• C_1-C_2 substituted by carbocyclic aryl,

••methoxy,

••methoxy substituted by carbocyclic aryl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

(ii) C_2-C_3 alkenyl substituted by substituent(s) independently selected from

•carbocyclic aryl,

•halogenated carbocyclic aryl,

•carbocyclic aryl substituted by nitro,

(iii) C_3-C_6 cycloalkyl,

C_3-C_6 cycloalkyl substituted by substituent(s) independently selected from

•methyl substituted by oxo,

•methyl substituted by carbocyclic aryl,

•carbocyclic aryl,

(iv) carbocyclyl,

(v) carbocyclic aryl,

carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•cyano,

•nitro,

•C_1-C_9 alkyl,

•C_1-C_9 alkyl substituted by substituent(s) independently selected from

••halogen,

••oxo,

••carbocyclic aryl,

••carbocyclic aryl substituted by methyl,

••carbocyclic aryloxy,

•C_1-C_7 alkoxy,

•halogenated C_1-C_7 alkoxy,

•C_1-C_7 alkoxy substituted by carbocyclic aryl,

•methylcarbonyloxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by methoxy,

•amino,

•di-methylamino,

•propargynylcarbonylamino substituted by carbocyclic aryl,

•carbocyclic arylsulfonylamino substituted by methyl,

•(carbocyclic aryl)NHC(O)NH substituted by halogenated methoxy,

•halogenated methylthio,

•carbocyclic arylthio substituted by cyano,

•di-propylamino sulfonyl,

•mono- or di- ethylaminocarbonyl substituted by carbocyclic aryl,

•carbocyclic aryl,

•heterocyclyl substituted by methyl,

•heterocyclyl substituted by halogenated carbocyclic aryl,

(vi) heterocyclyl,

or heterocyclyl substituted by substituent(s) independently selected from

•halogen,

•nitro,

•C_1-C_4 alkyl,

•C_1-C_4 alkyl substituted by substituent(s) independently selected from

••halogen,

••methylthio substituted by halogenated carbocyclic aryl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

••heterocyclyl,

•methoxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by methyl,

•C_1-C_3 alkylthio,

•propenylthio,

•carbocyclic arylthio,

•C_1-C_3 alkylsulfonyl,

•carbocyclic arylsulfonyl substituted by C_1-C_4 alkyl,

•carbocyclic aryl,

•halogenated carbocyclic aryl,

•carbocyclic aryl substituted by methyl,

•carbocyclic aryl substituted by nitro,

•heterocyclyl;

R_2 is methylamino or dimethylamino;

L is selected from Formula Va, VIIIa, or IXa;

wherein R_4 and R_5 are independently selected from H or C_1-C_3 alkyl;

Y is -C(O)-;

wherein carbocyclic aryl is phenyl, naphthyl, anthranyl, or biphenyl;

carbocyclyl is 1-oxo-indanyl, 9-oxo-fluorenyl, indenyl, anthraquinonyl, *C*-fluoren-9-ylidene, 1,2,3,4-tetrahydro-naphthyl, or bicyclo[2.2.1]hepteny;

heterocyclyl is 1,2,3-thiadiazolyl, 1,2,3-triazolyl, 1,2-dihydro-3-oxo-pyrazolyl, 1,3-dioxo-isoindolyl, 1*H*-indolyl, 1*H*-pyrrolyl, 1-oxo-3*H*-isobenzofuranyl, 2,3-dihydro-benzo[1,4]dioxinyl, 2,4-dihydro-3-oxo-pyrazolyl, 2*H*-benzopyranyl, 2-oxo-benzopyranyl, 3,4-dihydro-2*H*-benzo[b][1,4]dioxepinyl, 4-oxo-3,4-dihydro-phthalazinyl, 4-oxo-benzopyranyl, 9,10,10-trioxo-thioxanthenyl, 9*H*-xanthenyl, azetidinyl, benzimidazolyl, benzo[1,3]dioxolyl, benzo[2,1,3]oxadiazolyl, benzo[b]thienyl, furyl, imidazolyl, isoxazolyl, morpholino, morpholinyl, oxolanyl, piperidyl, piridyl, pyrazolyl, pyridyl, quinolyl, quinoxalyl, thiazolidyl, thiazolyl, thienyl, thiolanyl, 2,3-dihydro-1-oxo-isoindolyl, 2,3-dihydro-benzofuryl, 2-oxo-pyrrolidinyl, 4-oxo-1,5,6,7-tetrahydro-indolyl, cinnolyl, pyrimidyl, pyrrolidyl, tetrahydro-thienyl, benzofuranyl, or benzothiazolyl;

halogen is fluoro, chloro, bromo, or iodo.

Other more preferred compounds of this invention are those compounds of Formula I wherein,

Q is Formula II;

R_1 represents

(i) C_1-C_{10} alkyl substituted by substituent(s) independently selected from

•oxo,

•di-propylaminocarbonyl,

•methoxy substituted by carbocyclic aryl,

•methylcarbonyloxy,

•carbocyclic aryloxy,

•halogenated carbocyclic aryloxy,

•carbocyclic aryloxy substituted by nitro,

•heterocyclyloxy substituted by methyl,

•substituted heterocyclyl-ethylideneaminooxy,

•*tert*-butoxycarbonylamino,

•carbocyclic arylcarbonylamino,

•C_1-C_2 alkylthio,

•C_1-C_2 alkylthio substituted by substituent(s) independently selected from

••halogenated carbocyclic aryl,

••carbocyclic aryl substituted by methoxy,

•carbocyclic arylthio,

•hetrocyclylthio substituted by nitro,

•hetrocyclylthio substituted by methyl,

•C_5-C_6 cycloalkenyl,

•carbocyclyl substituted by substituent(s) independently selected from

••halogen,

••methyl,

••methoxy,

••ethenyl substituted by carbocyclic aryl substituted methylsulfinyl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••nitro,

••C_1-C_4 alkyl,

••C_1-C_4 alkyl substituted by substituent(s) independently selected from

•••oxo,

•••carbocyclic aryl,

•••heterocyclyl,

••C_1-C_4 alkoxy,

••halogenated C_1-C_4 alkoxy,

••C_1-C_4 alkoxy substituted by carbocyclic aryl,

••carbocyclic aryloxy,

••halogenated mono-carbocyclic arylaminocarbonyl,

••carbocyclic aryl,

••heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••C_1-C_2 alkyl,

•• C_1-C_2 substituted by carbocyclic aryl,

••methoxy,

••methoxy substituted by carbocyclic aryl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

(ii) C_2-C_3 alkenyl substituted by substituent(s) independently selected from

•carbocyclic aryl,

•halogenated carbocyclic aryl,

•carbocyclic aryl substituted by nitro,

(iii) C_3-C_6 cycloalkyl substituted by substituent(s) independently selected from

•methyl substituted by oxo,

•methyl substituted by carbocyclic aryl,

•carbocyclic aryl,

(iv) carbocyclyl,

(v) carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•cyano,

•nitro,

•C_1-C_9 alkyl,

•C_1-C_9 alkyl substituted by substituent(s) independently selected from

••halogen,

••oxo,

••carbocyclic aryl,

••carbocyclic aryl substituted by methyl,

••carbocyclic aryloxy,

•C_1-C_7 alkoxy,

•halogenated C_1-C_7 alkoxy,

•C_1-C_7 alkoxy substituted by carbocyclic aryl,

•methylcarbonyloxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by methoxy,

•amino,

•di-methylamino,

•propargynylcarbonylamino substituted by carbocyclic aryl,

•carbocyclic arylsulfonylamino substituted by methyl,

•(carbocyclic aryl)NHC(O)NH substituted by halogenated methoxy,

•halogenated methylthio,

•carbocyclic arylthio substituted by cyano,

•di-propylamino sulfonyl,

•mono- or di- ethylaminocarbonyl substituted by carbocyclic aryl,

•carbocyclic aryl,

•heterocyclyl substituted by methyl,

•heterocyclyl substituted by halogenated carbocyclic aryl,

(vi) or heterocyclyl substituted by substituent(s) independently selected from

•halogen,

•nitro,

•C_1-C_4 alkyl,

•C_1-C_4 alkyl substituted by substituent(s) independently selected from

••halogen,

••methylthio substituted by halogenated carbocyclic aryl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

••heterocyclyl,

•methoxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by methyl,

•C_1-C_3 alkylthio,

•propenylthio,

•carbocyclic arylthio,

•C_1-C_3 alkylsulfonyl,

•carbocyclic arylsulfonyl,

•carbocyclic arylsulfonyl substituted by C_1-C_4 alkyl,

•carbocyclic aryl,

•halogenated carbocyclic aryl,

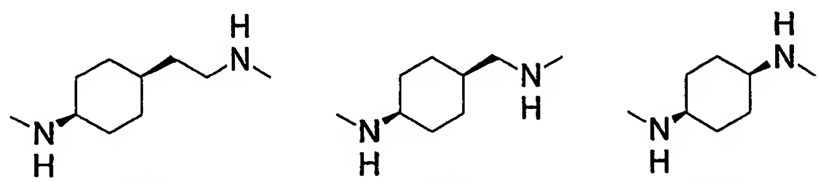
•carbocyclic aryl substituted by methyl,

•carbocyclic aryl substituted by nitro,

•heterocyclyl;

R_2 is methylamino or dimethylamino;

L is selected from Formula XX - XXII;



XX XXI XXII

Y is -C(O)-;

wherein carbocyclic aryl is phenyl, naphthyl, or biphenyl;

carbocyclyl is 1-oxo-indanyl, 9-oxo-fluorenyl, indenyl, anthraquinonyl, *C*-fluoren-9-ylidene, 1,2,3,4-tetrahydro-naphthyl, or bicyclo[2.2.1]hepteny;

heterocyclyl is 1,2,3-thiadiazolyl, 1,2,3-triazolyl, 1,2-dihydro-3-oxo-pyrazolyl, 1*H*-indolyl, 1*H*-pyrrolyl, 2,4-dihydro-3-oxo-pyrazolyl, 2*H*-benzopyranyl, 4-oxo-benzopyranyl, azetidinyl, benzo[b]thienyl, furyl, isoxazolyl, morpholinyl, piperidyl, piridyl, pyrazolyl, pyridyl, quinolyl, thiazolidyl, thiazolyl, thienyl, thiolanyl, 2,3-dihydro-1-oxo-isoindolyl, 2,3-dihydro-benzofuryl, 2-oxo-benzopyranyl, 2-oxo-pyrrolidinyl, 4-oxo-1,5,6,7-tetrahydro-indolyl, 9*H*-xanthenyl, cinnolyl, imidazolyl, morpholino, pyrimidyl, pyrrolidyl, tetrahydro-thienyl, benzofuranyl, or benzothiazolyl;

halogen is fluoro, chloro, bromo, or iodo.

Further other more preferred compounds of this invention are those compounds of Formula I wherein,

Q is Formula II;

R_1 represents

(i) C_1-C_5 alkyl substituted by substituent(s) independently selected from

•oxo,

•di-propylaminocarbonyl,

•methoxy substituted by carbocyclic aryl,

•methylcarbonyloxy,

•carbocyclic aryloxy,

•halogenated carbocyclic aryloxy,

•carbocyclic aryloxy substituted by nitro,

•heterocyclyloxy substituted by methyl,

•substituted heterocyclyl-ethylideneaminooxy,

•*tert*-butoxycarbonylamino,

•carbocyclic arylcarbonylamino,

•C_1-C_2 alkylthio,

•C_1-C_2 alkylthio substituted by substituent(s) independently selected from

••halogenated carbocyclic aryl,

••carbocyclic aryl substituted by methoxy,

•carbocyclic arylthio,

•hetrocyclylthio substituted by nitro,

•hetrocyclylthio substituted by methyl,

•cyclohexenyl,

•carbocyclyl substituted by substituent(s) independently selected from

••halogen,

••methyl,

••methoxy,

••ethenyl substituted by carbocyclic aryl substituted methylsulfinyl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••nitro,

•• C_1-C_4 alkyl,

••C_1-C_4 alkyl substituted by substituent(s) independently selected from

•••oxo,

•••carbocyclic aryl,

•••heterocyclyl,

••C_1-C_2 alkoxy,

••halogenated C_1-C_2 alkoxy,

••C_1-C_2 alkoxy substituted by carbocyclic aryl,

••carbocyclic aryloxy,

••halogenated mono-carbocyclic arylaminocarbonyl,

••carbocyclic aryl,

••heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••C_1-C_2 alkyl,

•• C_1-C_2 substituted by carbocyclic aryl,

••methoxy,

••methoxy substituted by carbocyclic aryl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

(ii) C_2-C_3 alkenyl substituted by substituent(s) independently selected from

•carbocyclic aryl,

•halogenated carbocyclic aryl,

•carbocyclic aryl substituted by nitro,

(iii) C_3-C_6 cycloalkyl substituted by substituent(s) independently selected from

•methyl substituted by oxo,

•methyl substituted by carbocyclic aryl,

•carbocyclic aryl,

(iv) carbocyclyl,

(v) carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•cyano,

•nitro,

•C_1-C_4 alkyl,

•C_1-C_2 alkyl substituted by substituent(s) independently selected from

••halogen,

••oxo,

••carbocyclic aryl,

••carbocyclic aryl substituted by methyl,

••carbocyclic aryloxy,

•C_1-C_2 alkoxy,

•halogenated C_1-C_2 alkoxy,

•C_1-C_2 alkoxy substituted by carbocyclic aryl,

•methylcarbonyloxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by methoxy,

•amino,

•di-methylamino,

•propargynylcarbonylamino substituted by carbocyclic aryl,

•carbocyclic arylsulfonylamino substituted by methyl,

•(carbocyclic aryl)NHC(O)NH substituted by halogenated methoxy,

•halogenated methylthio,

•carbocyclic arylthio substituted by cyano,

•di-propylamino sulfonyl,

•mono- or di- ethylaminocarbonyl substituted by carbocyclic aryl,

•carbocyclic aryl,

•heterocyclyl substituted by methyl,

•heterocyclyl substituted by halogenated carbocyclic aryl,

(vi) or heterocyclyl substituted by substituent(s) independently selected from

•halogen,

•nitro,

•C_1-C_4 alkyl,

•C_1-C_4 alkyl substituted by substituent(s) independently selected from

••halogen,

••methylthio substituted by halogenated carbocyclic aryl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

••heterocyclyl,

•methoxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by methyl,

•C_1-C_3 alkylthio,

•propenylthio,

•carbocyclic arylthio,

•C_1-C_3 alkylsulfonyl,

•carbocyclic arylsulfonyl,

•carbocyclic arylsulfonyl substituted by methyl,

•carbocyclic aryl,

•halogenated carbocyclic aryl,

•carbocyclic aryl substituted by methyl,

•carbocyclic aryl substituted by nitro,

•heterocyclyl;

R_2 is methylamino or dimethylamino;

L is selected from Formula XX - XXII;

Y is -C(O)-;

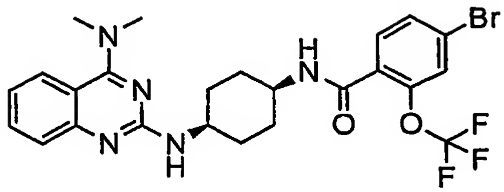
wherein carbocyclic aryl is phenyl , naphthyl, or biphenyl;

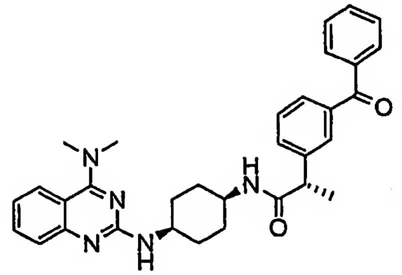
carbocyclyl is 1-oxo-indanyl, indenyl, 9-oxo-fluorenyl, 1,2,3,4-tetrahydro-naphthyl, or bicyclo[2.2.1]hepteny;

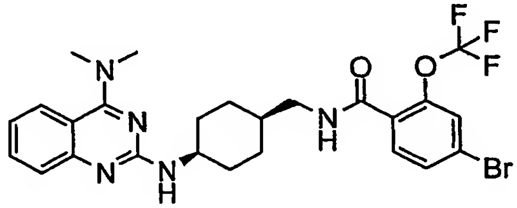
heterocyclyl is 1*H*-indolyl, 2,4-dihydro-3-oxo-pyrazolyl, furyl, pyrazolyl, pyridyl, thienyl, 1,2,3-triazolyl, 1*H*-pyrrolyl, 2,3-dihydro-1-oxo-isoindolyl, 2,3-dihydro-benzofuryl, 2*H*-benzopyranyl, 2-oxo-benzopyranyl, 4-oxo-1,5,6,7-tetrahydro-indolyl, imidazolyl, isoxazolyl, morpholino, morpholinyl, pyrazolyl, pyrimidyl, quinolyl, thiazolyl, tetrahydro-thienyl, benzofuranyl, or benzothiazolyl;

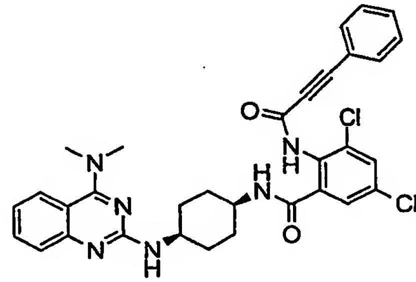
halogen is fluoro, chloro, bromo, or iodo.

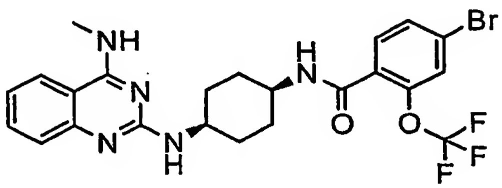
The following compounds are specially preffered;

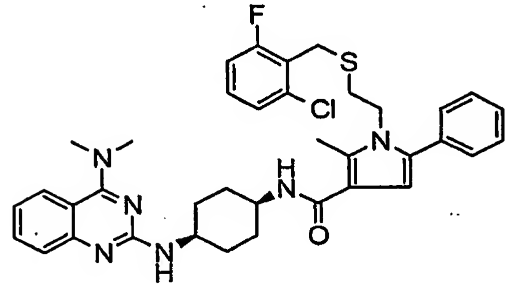
 ,

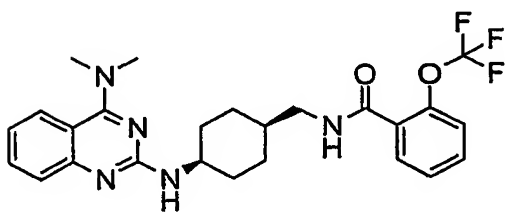
 ,

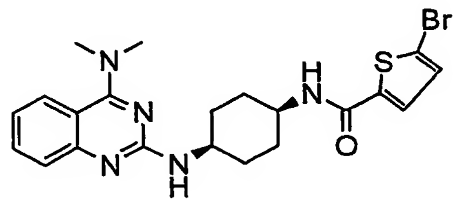
 ,

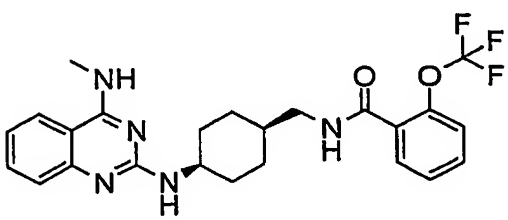
 ,

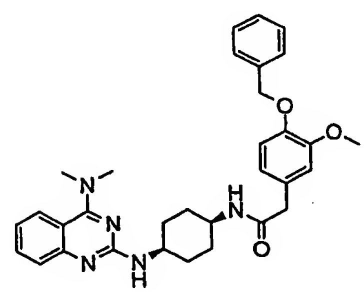
 ,

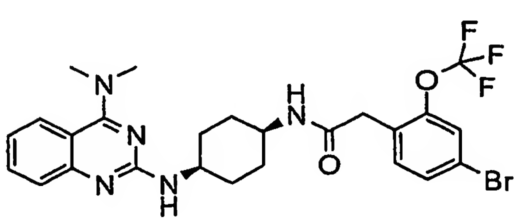
 ,

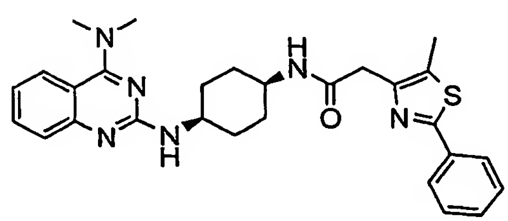
 ,

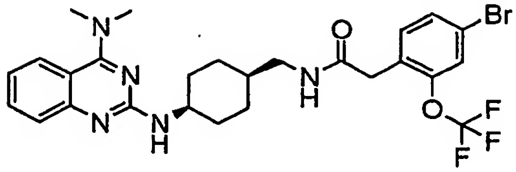
 ;

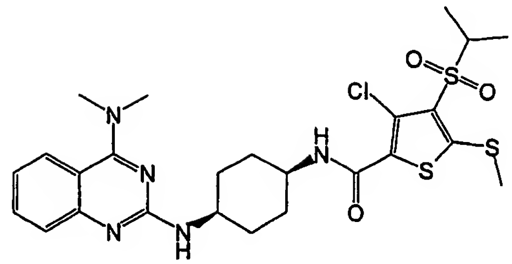
 ,

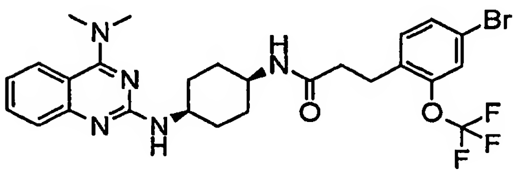
 ,

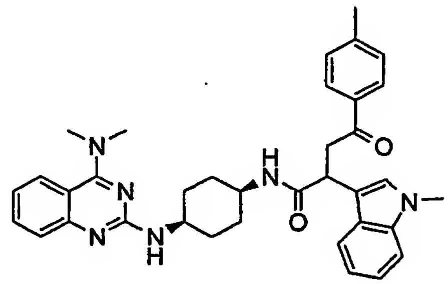
 ,

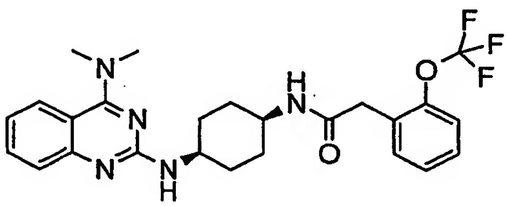
 ,

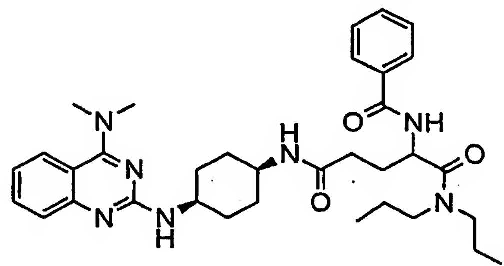
 ,

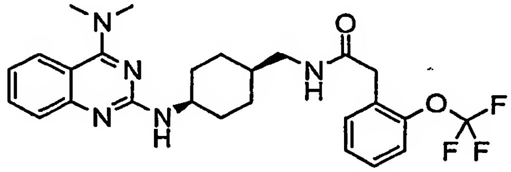
 ,

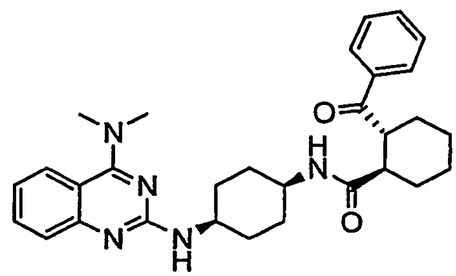
 ,

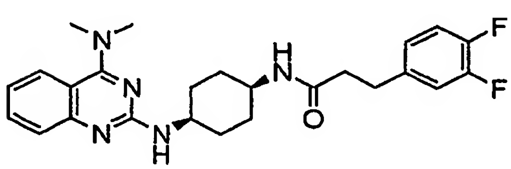
 ,

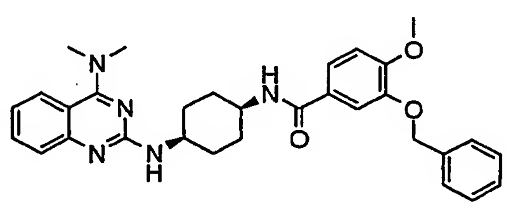
 ,

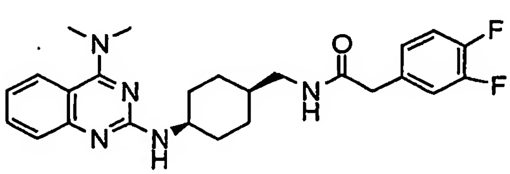
 ,

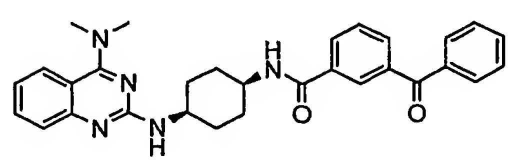
 ,

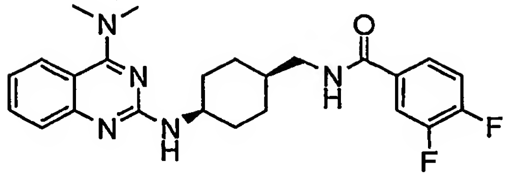
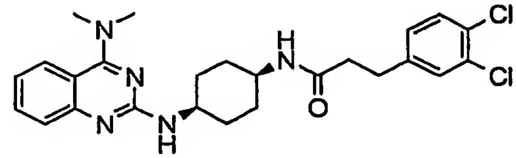
 ,

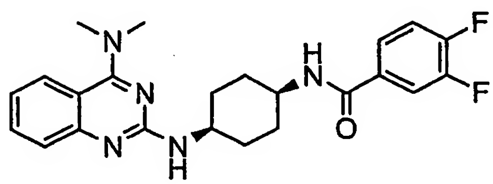
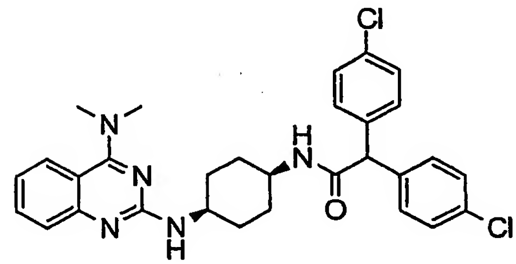
 ,

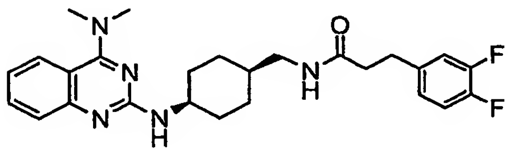
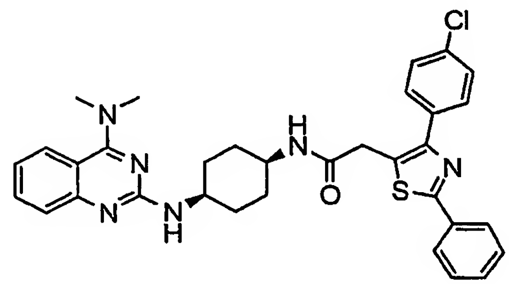
 ,

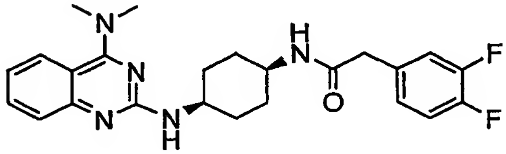
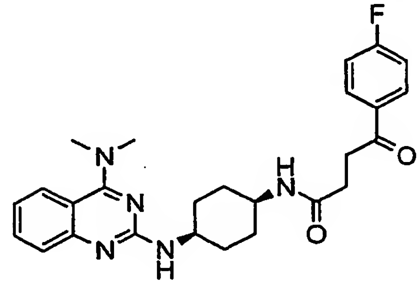
 ,

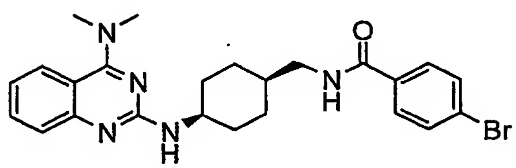
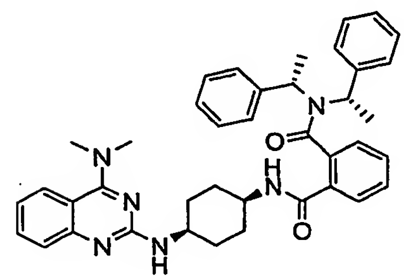
 ,

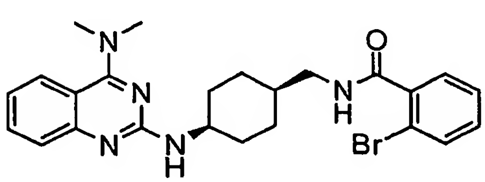
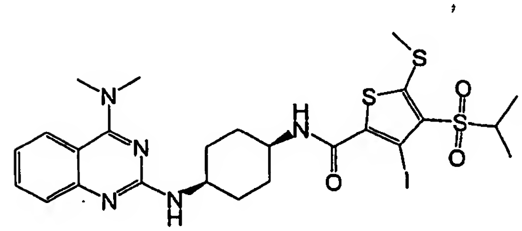
 ,  ,

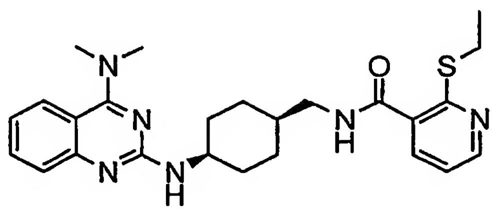
 ,  ,

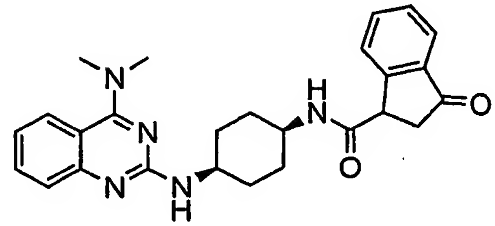
 ,  ,

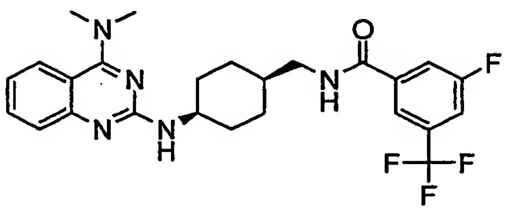
 ,  ,

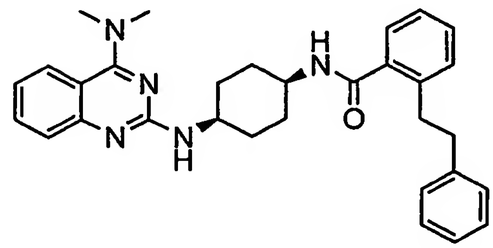
 ,  ,

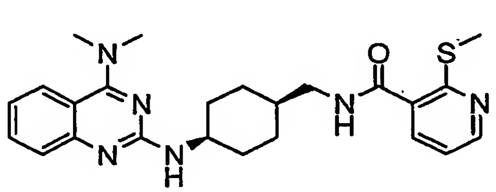
 ,  ,

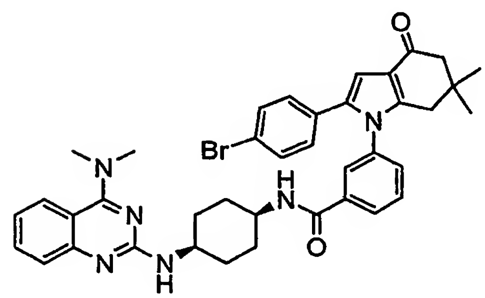

,

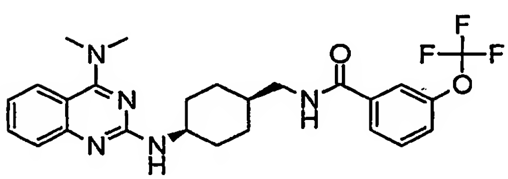

,

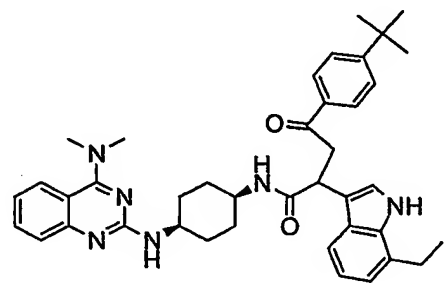

,

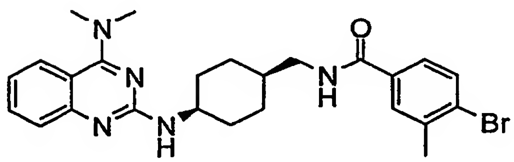

,

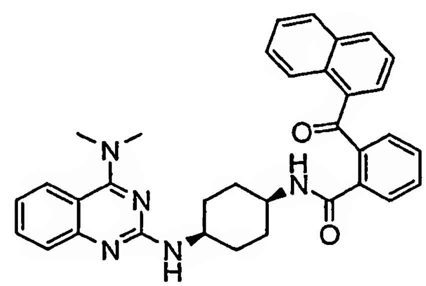

,

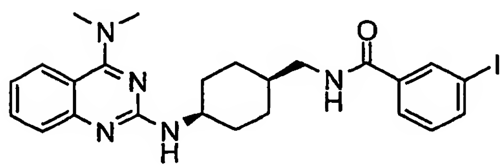

,

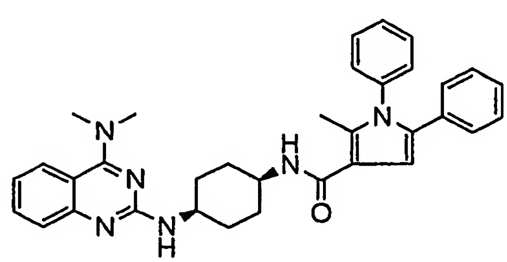

,

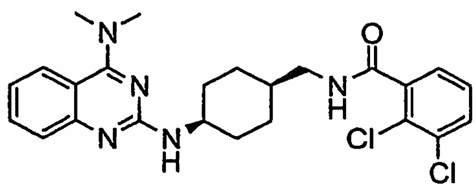

,

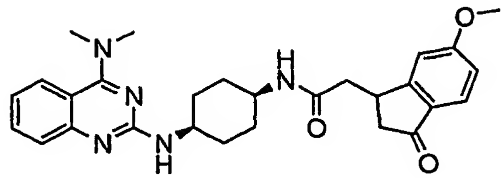

,

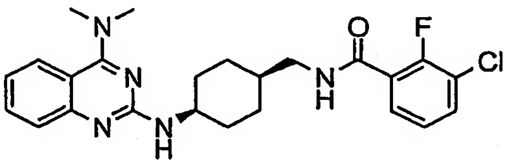

,

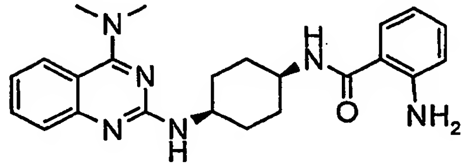

,

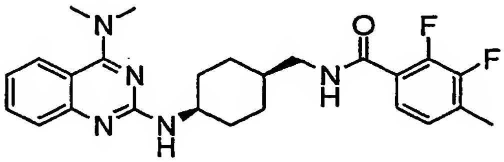

,

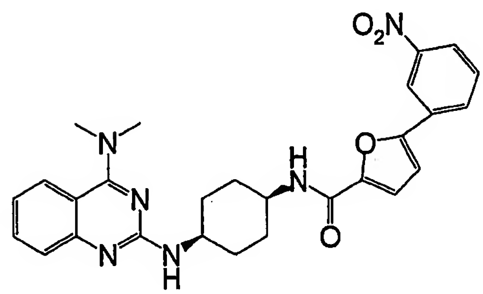
 ,

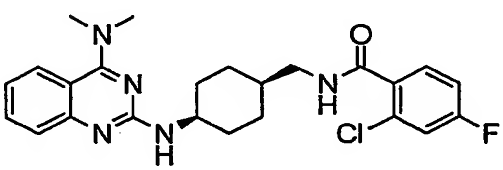
 ,

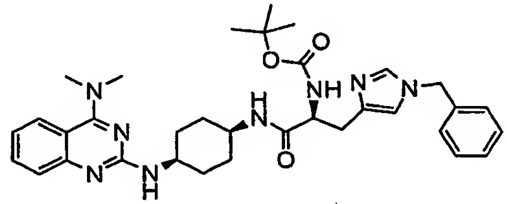
 ,

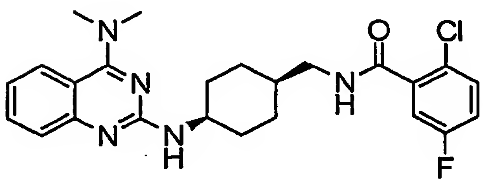
 ,

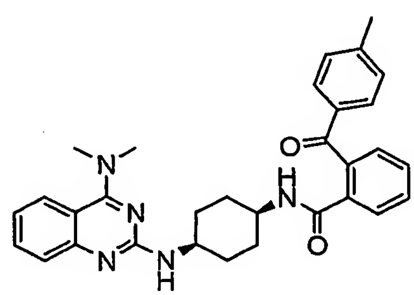
 ,

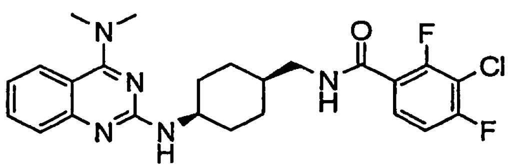
 ,

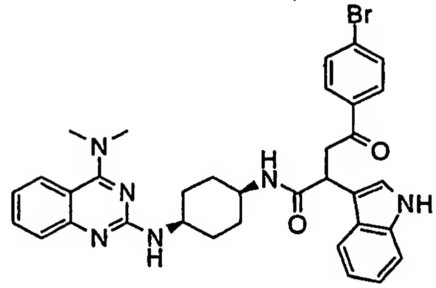
 ,

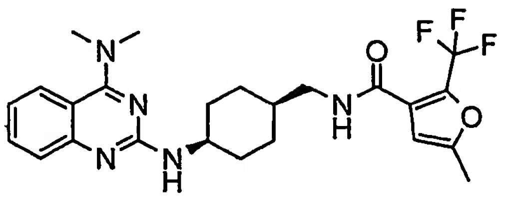
 ,

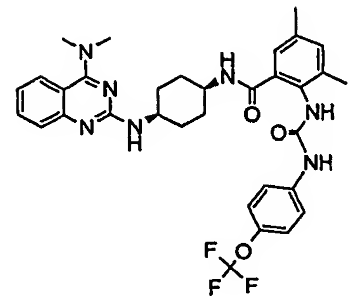
 ,

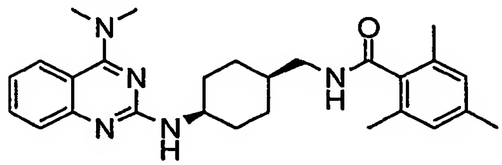
 ,

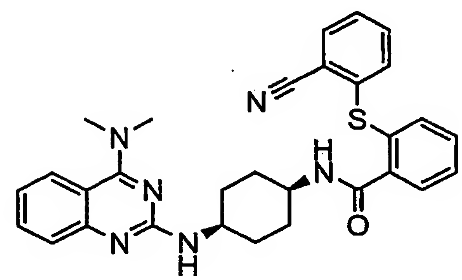
 ,

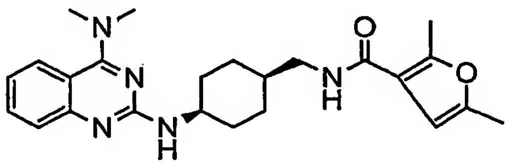
 ,

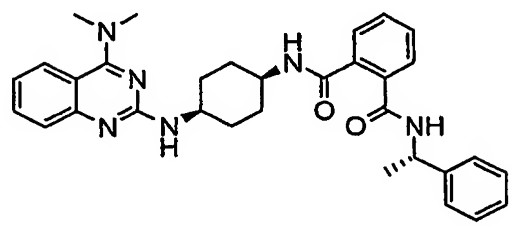
 ,

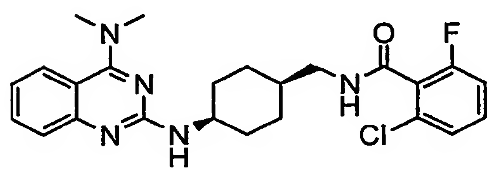
 ,

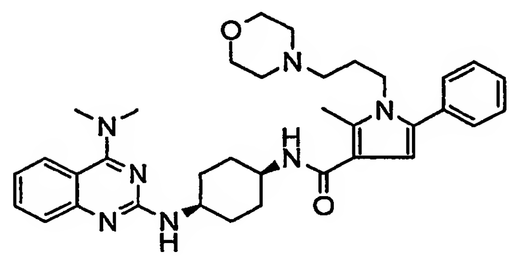
 ,

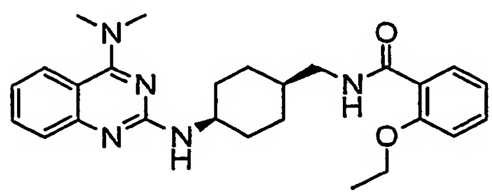
 ,

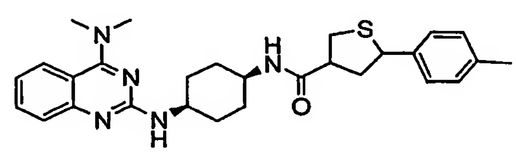
 ,

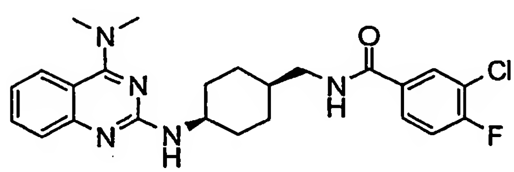
 ,

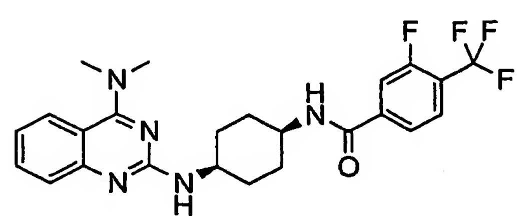
 ,

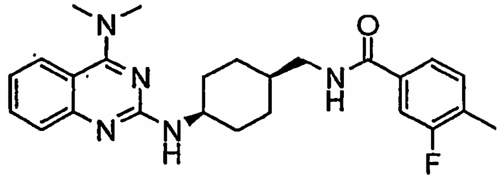
 ,

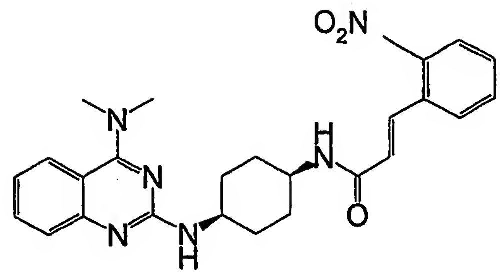
 ,

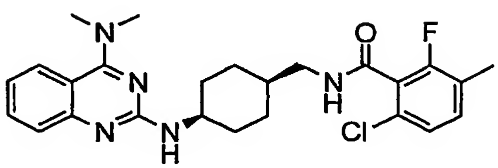
 ,

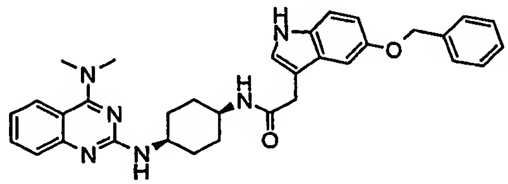
 ,

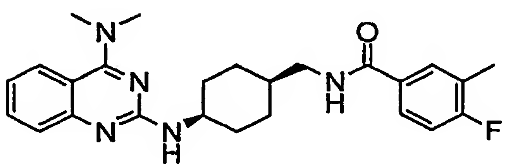
 ,

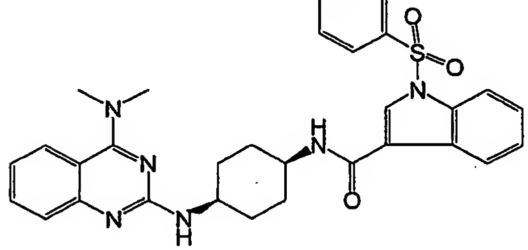
 ,

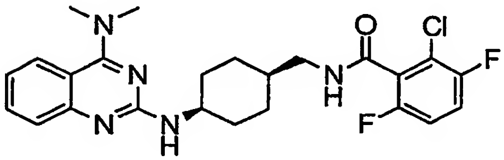
 ,

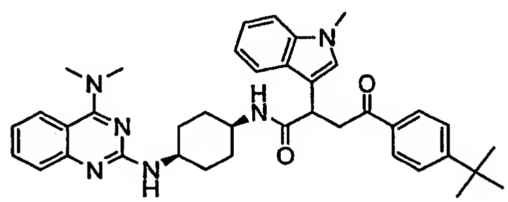
 ,

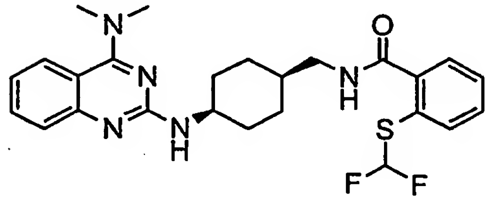
 ,

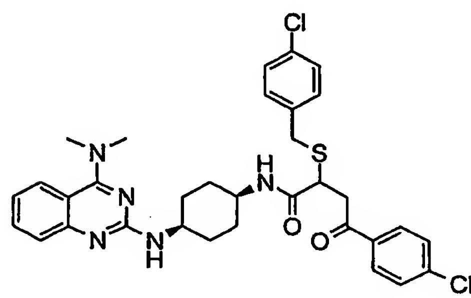
 ,

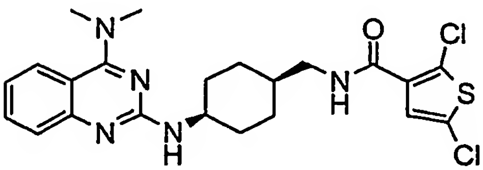
 ,

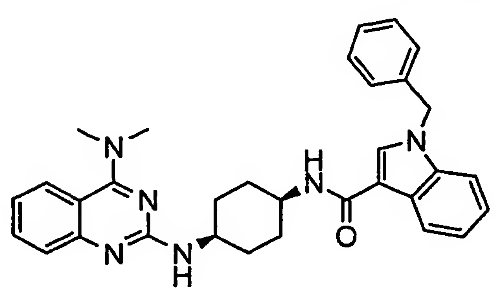
 ,

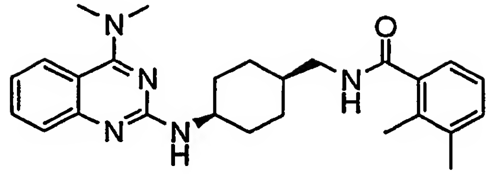
 ,

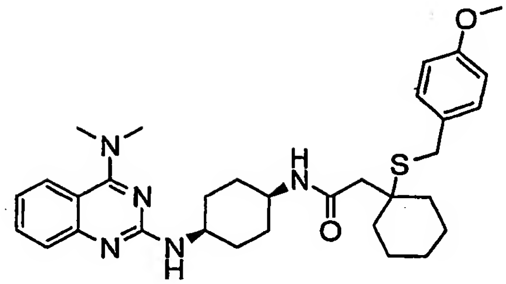
 ,

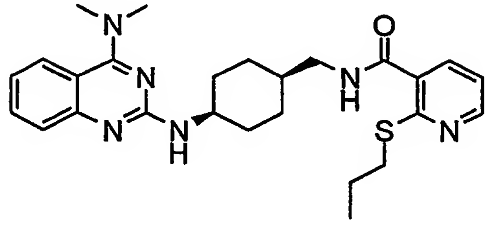
 ,

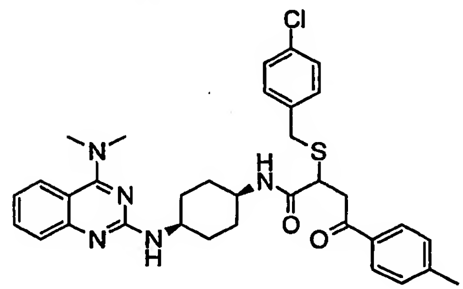
 ,

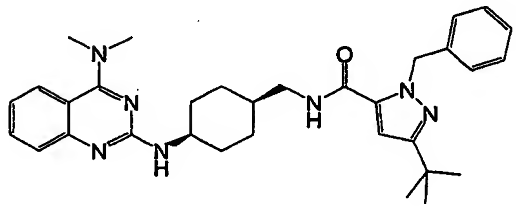
 ,

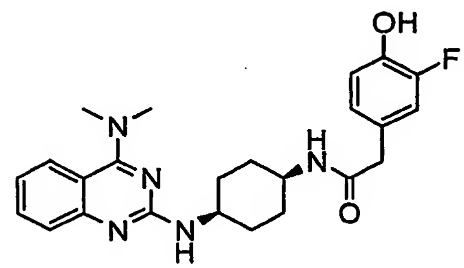

,

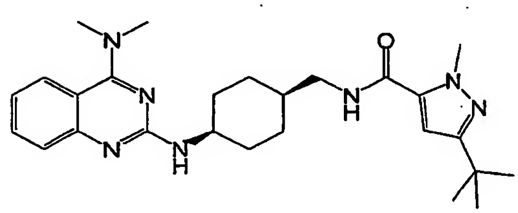

,

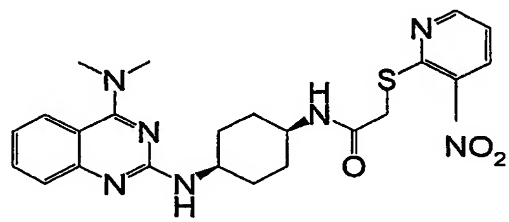

,

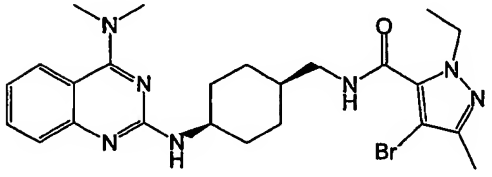

,

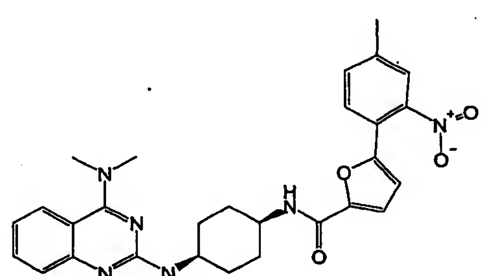

,

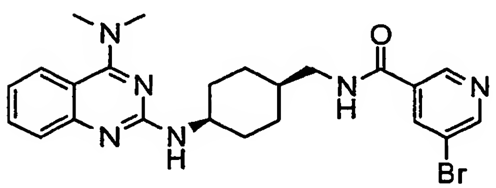

,

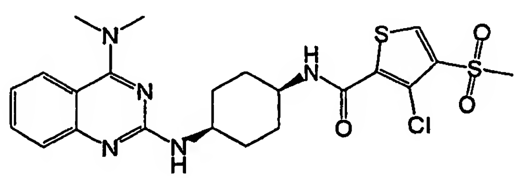

,

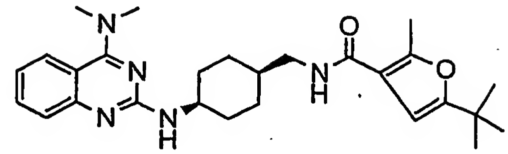

,

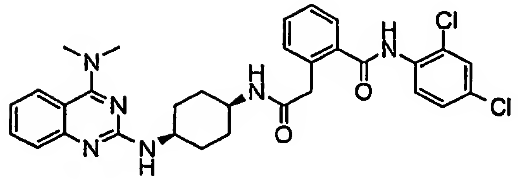

,

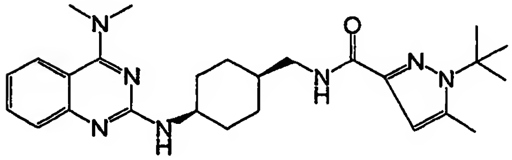

,

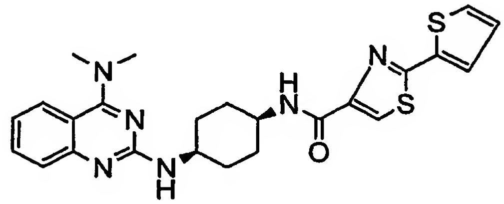

,

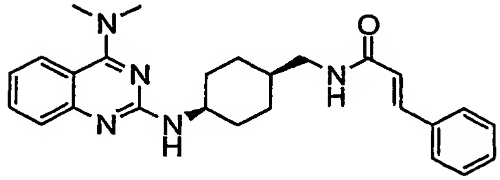

,

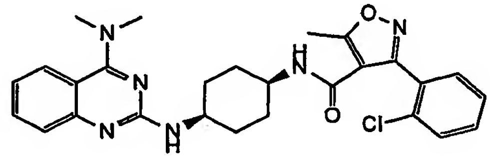
 ,

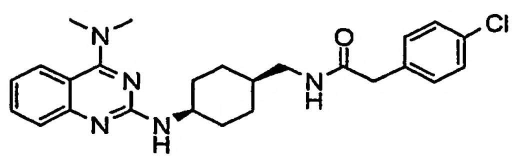
 ,

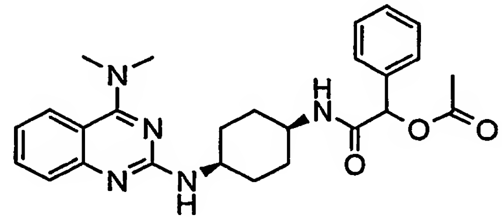
 ,

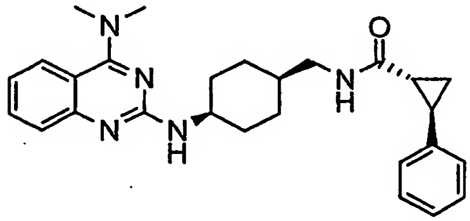
 ,

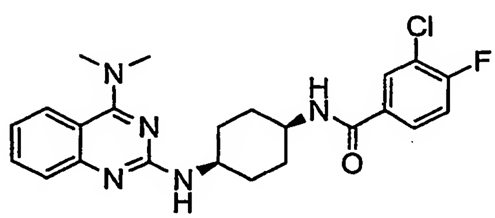
 ,

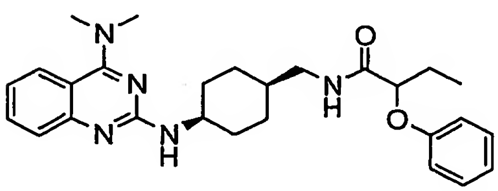
 ,

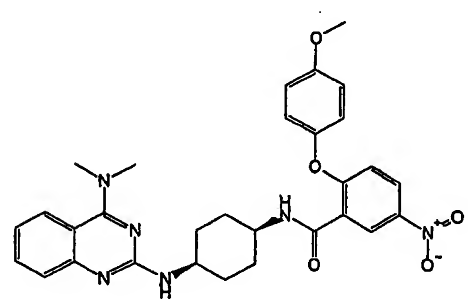
 ,

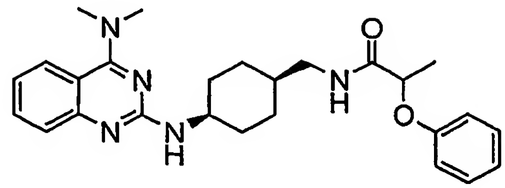
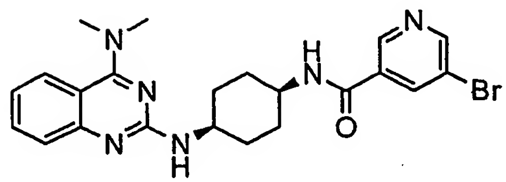
 ,

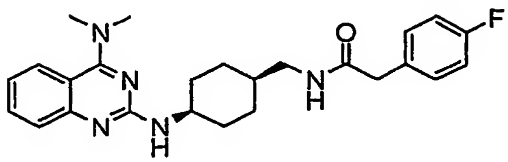
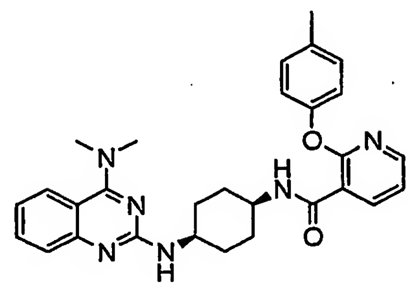
 ,

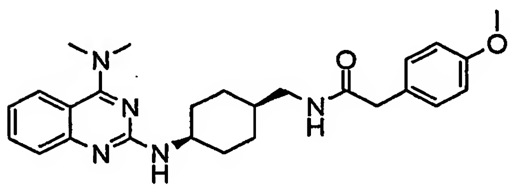
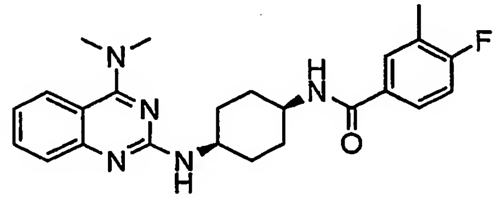
 ,

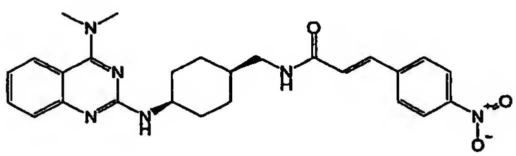
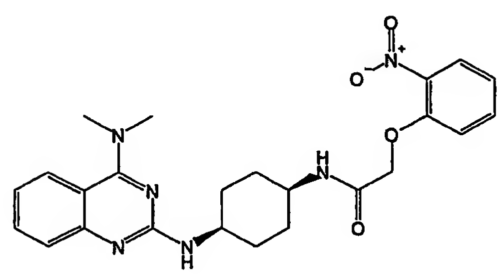
 ,

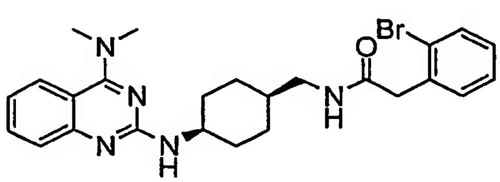
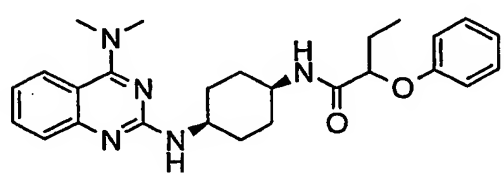
 ,

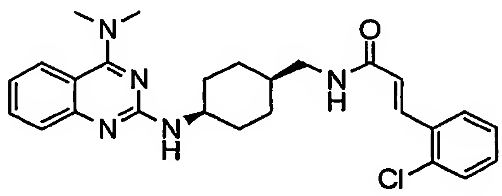
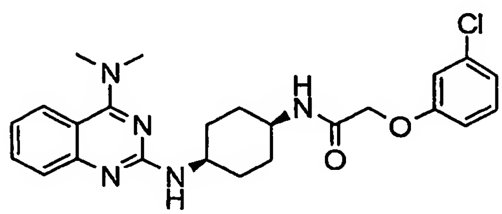
,
,

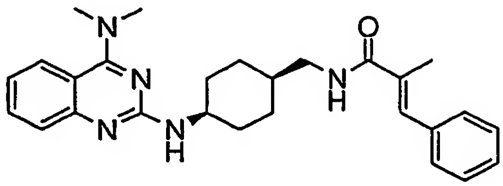
,
,

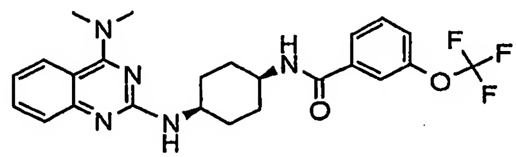
,
,

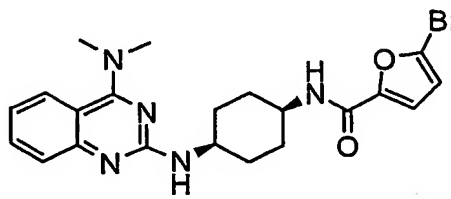
,
,

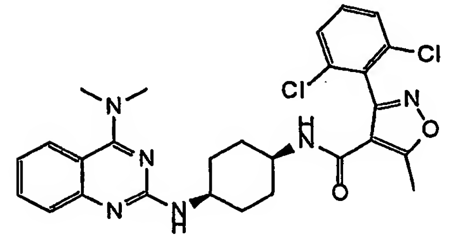
,
,

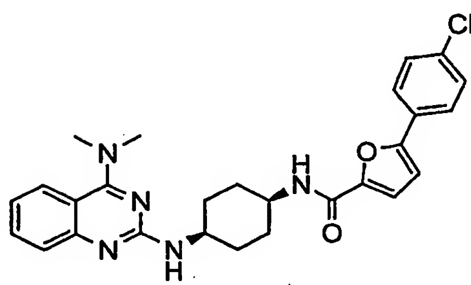
,
,

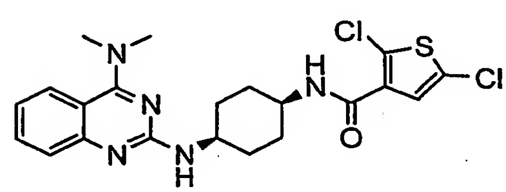
 ,

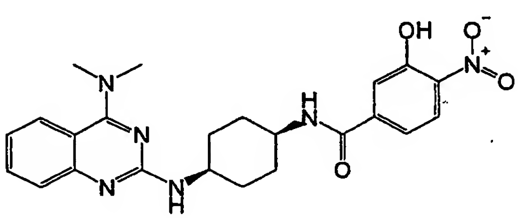
 ,

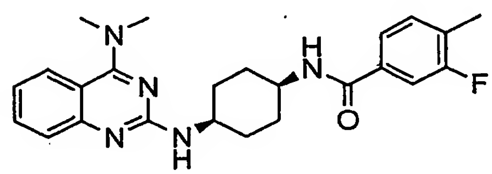
 ,

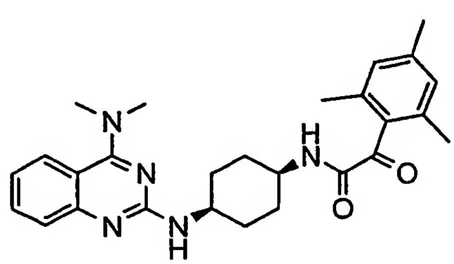
 ,

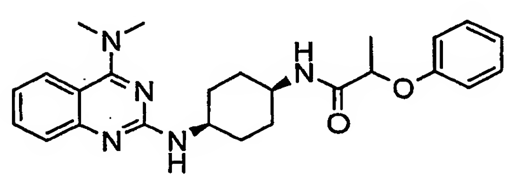
 ,

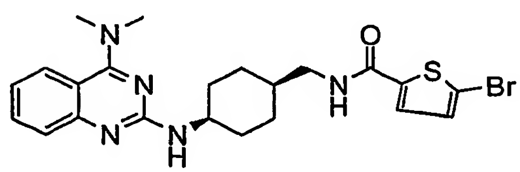
 ,

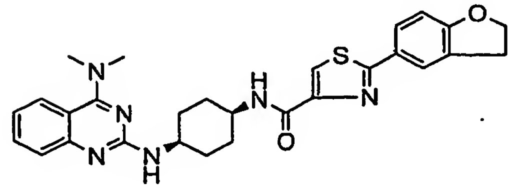
 ,

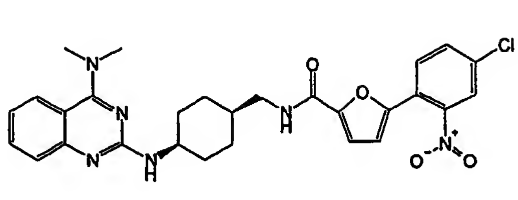
 ,

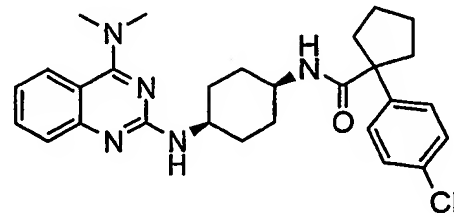
 ,

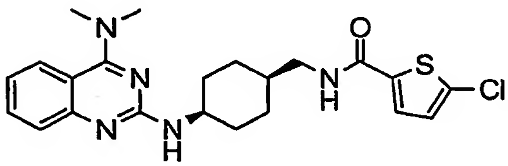
 ,

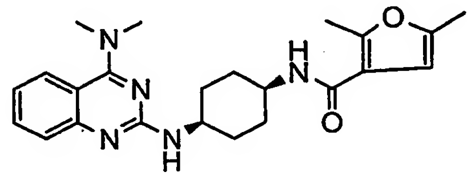
 ,

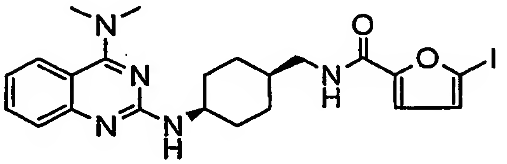
 ,

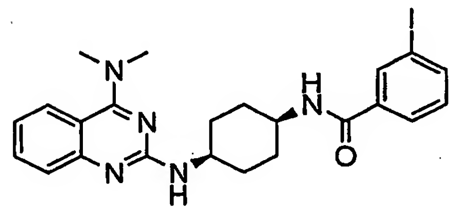
 ,

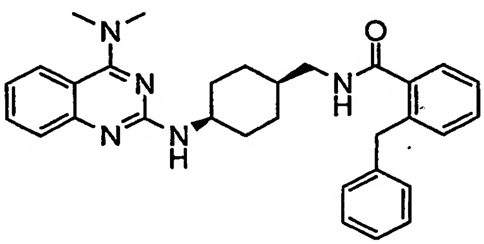
 ,

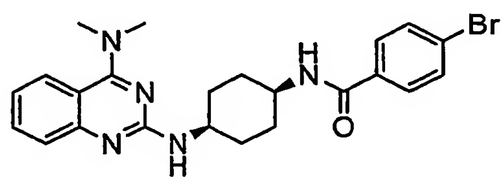
 ,

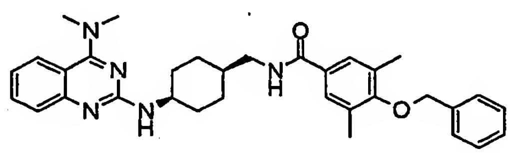
 ,

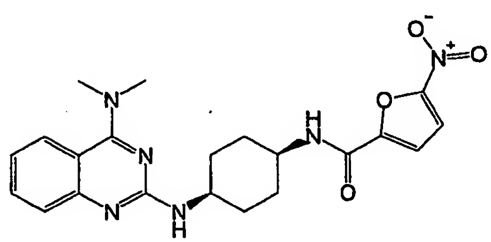
 ,

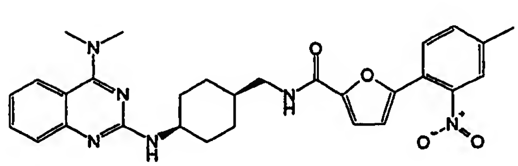
 ,

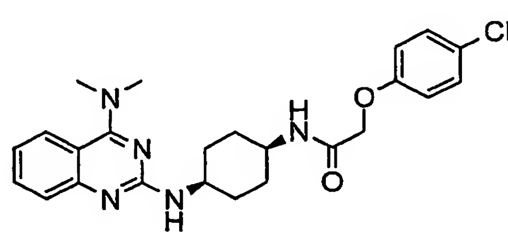
 ,

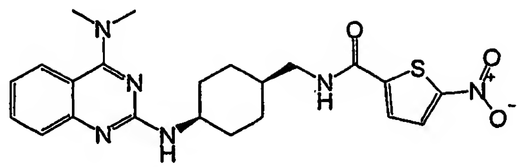
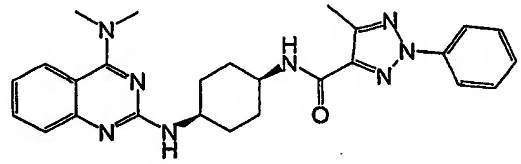
 ,

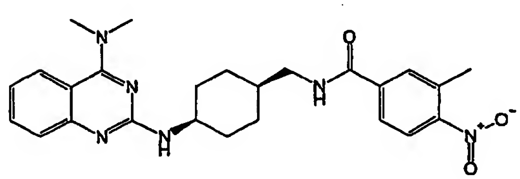
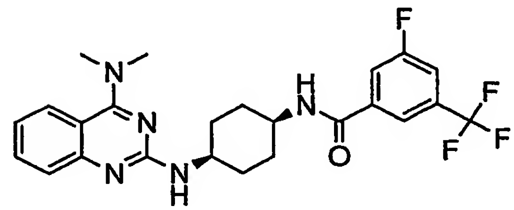
 ,

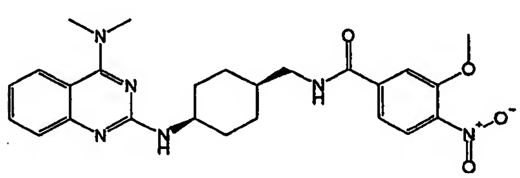
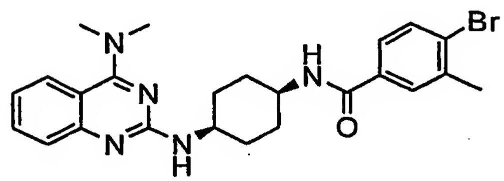
 ,

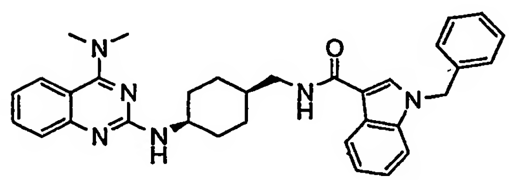
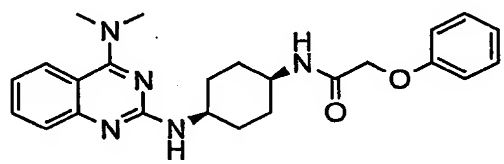
 ,

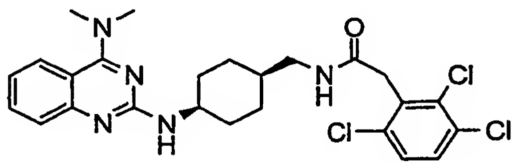
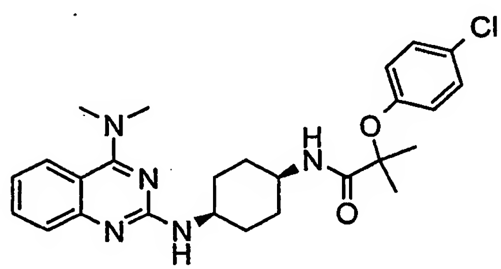
 ,

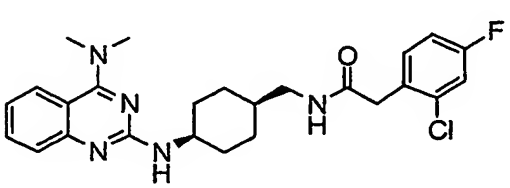
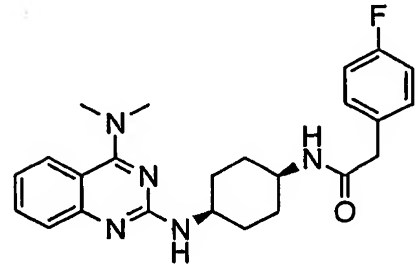
 ,  ,

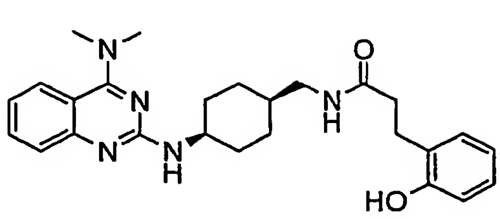
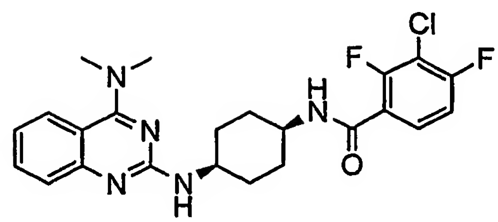
 ,  ,

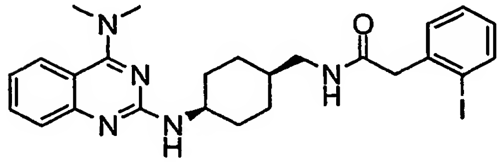
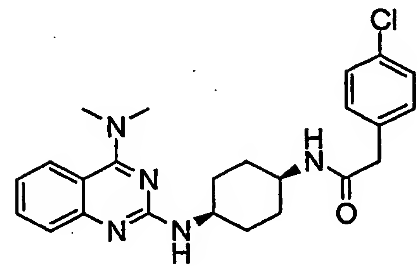
 ,  ,

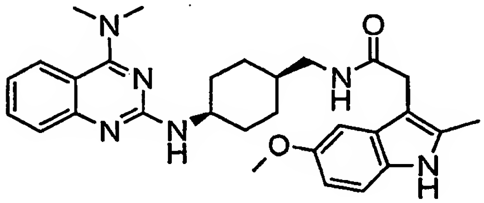
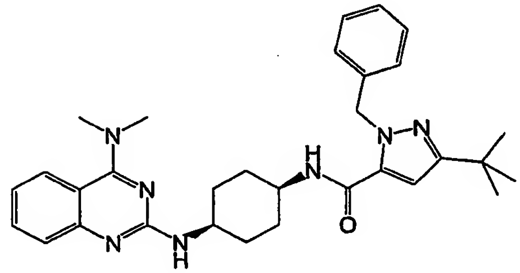
 ,  ,

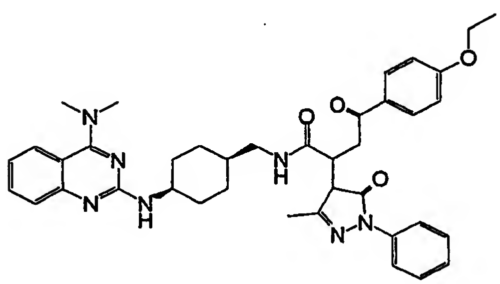
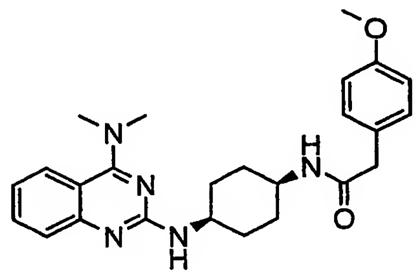
 ,  ,

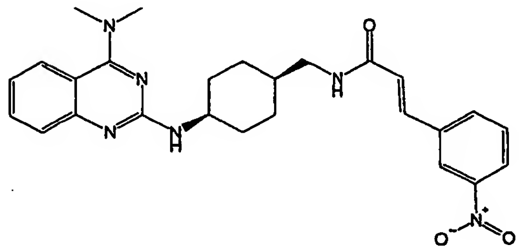
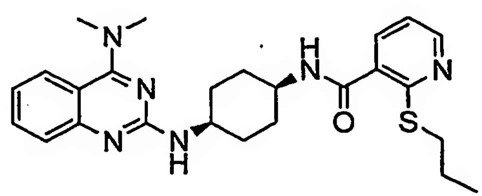
 ,  ,

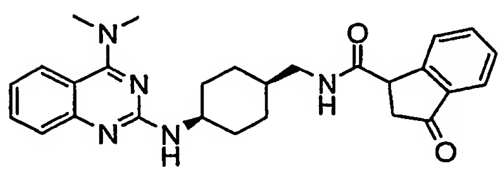
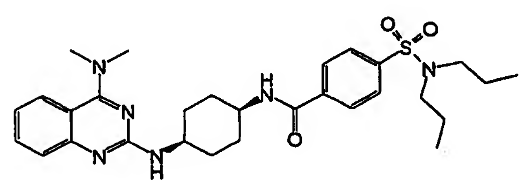
 ,  ,

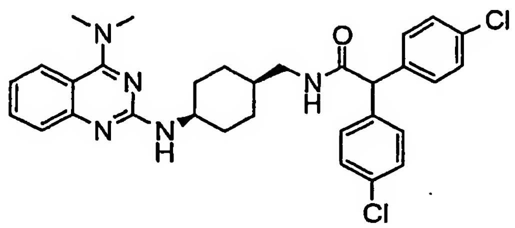
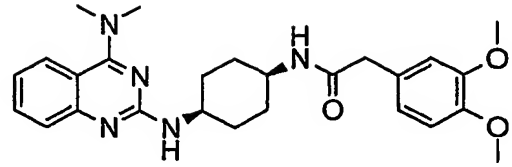
 ,  ,

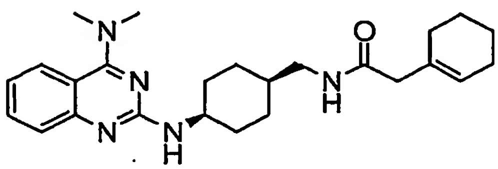
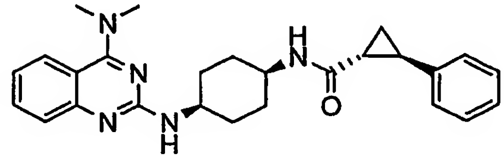
 ,  ,

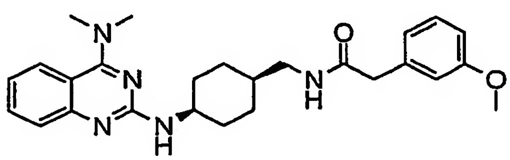
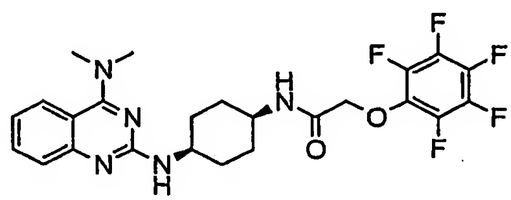
 ,  ,

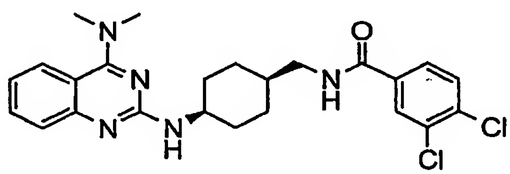
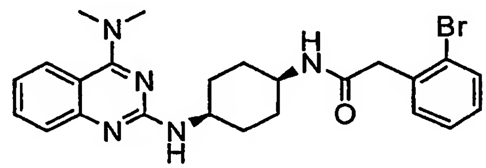
 ,  ,

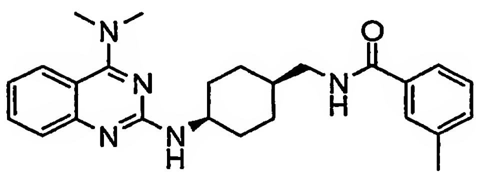
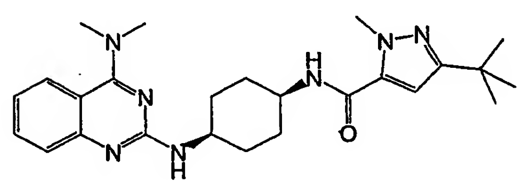
 ,  ,

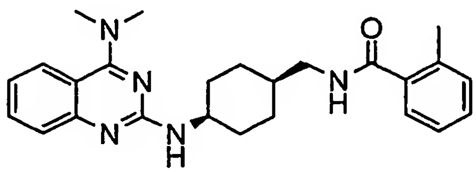
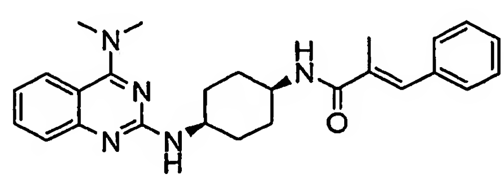
 ,  ,

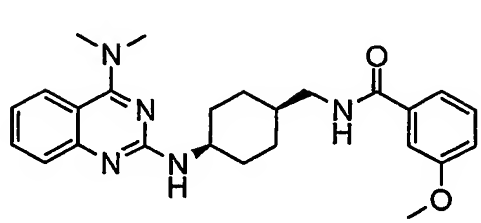
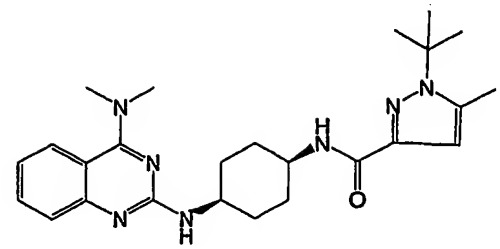
 ,  ,

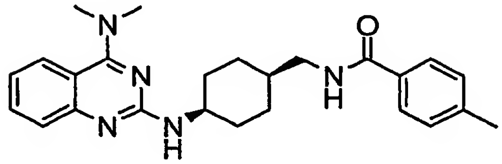
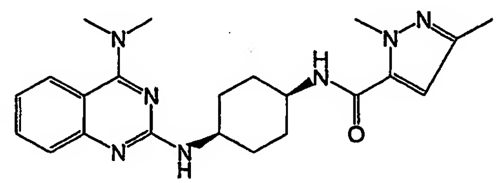
 ,  ,

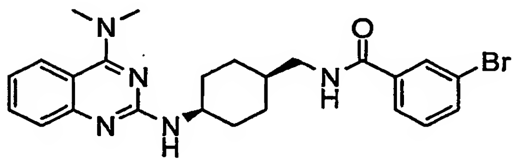
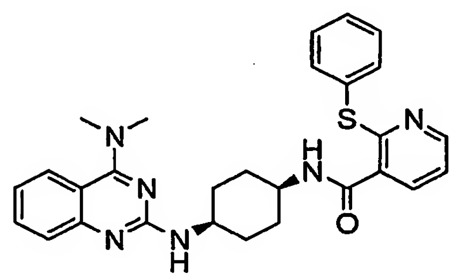
 ,  ,

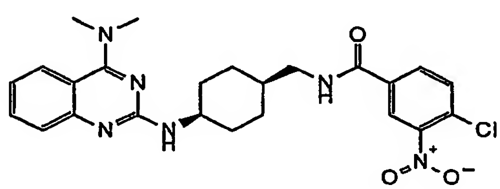
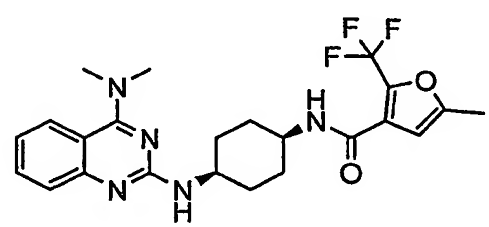
 ,  ,

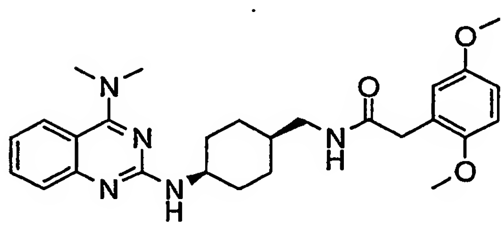
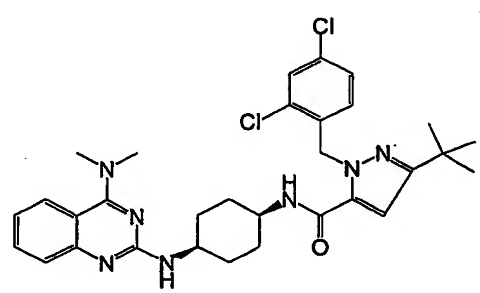
 ,  ,

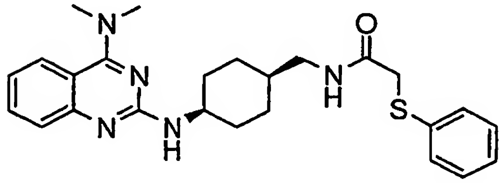
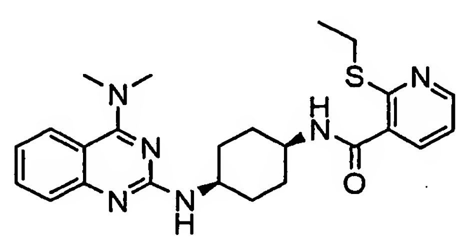
 ,  ,

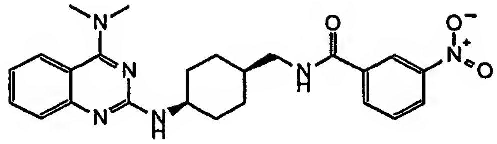
 ,  ,

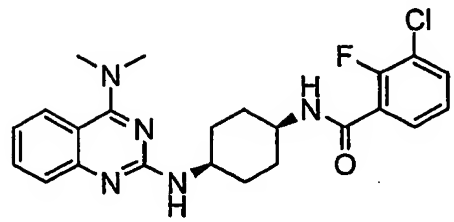
 ,  ,

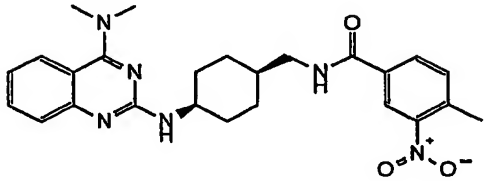
 ,  ,

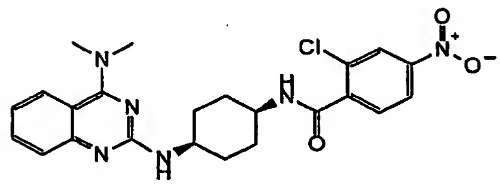
 ,  ,

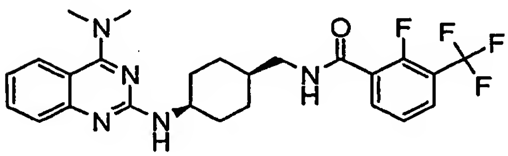
 ,  ,

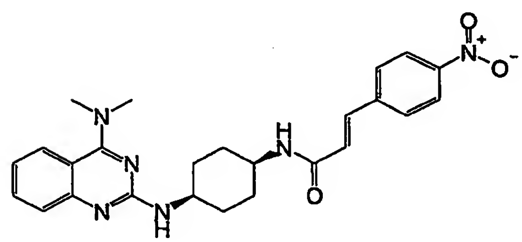
 ,

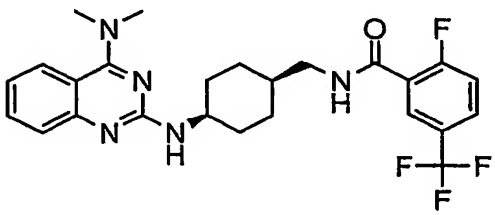
 ,

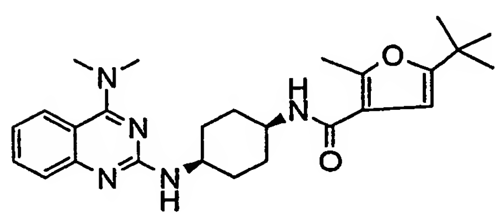
 ,

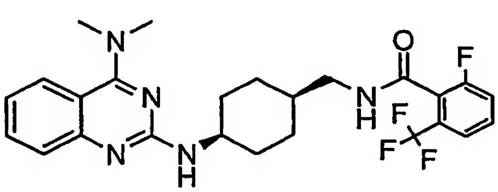
 ,

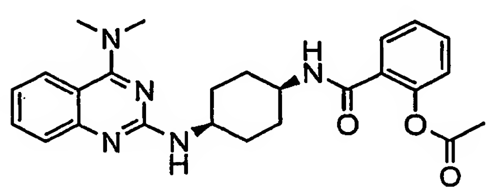
 ,

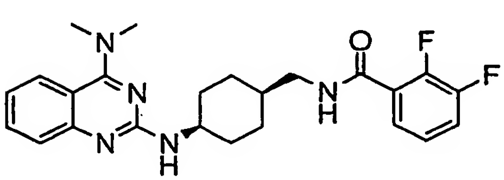
 ,

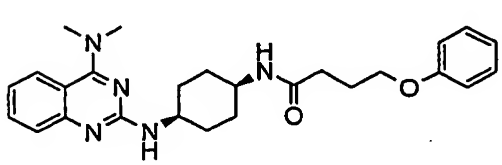
 ,

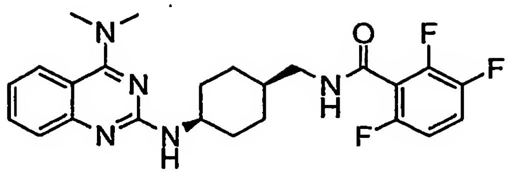
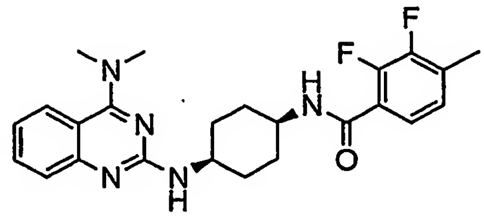
 ,

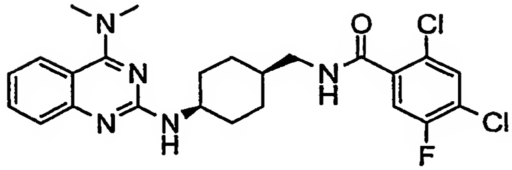
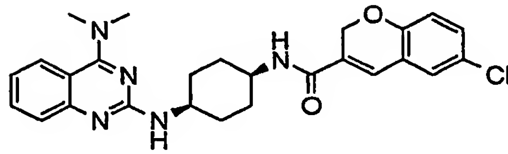
 ,

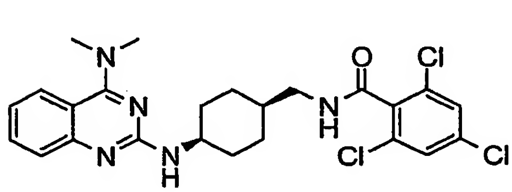
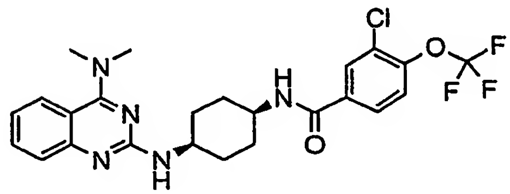
 ,

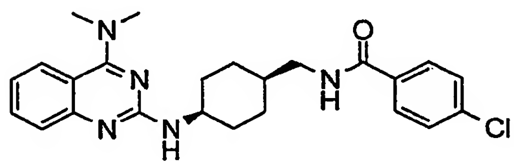
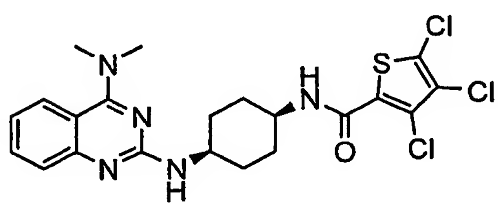
 ,

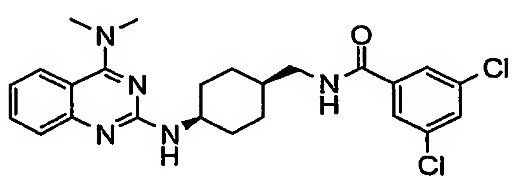
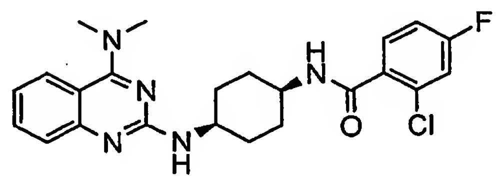
 ,

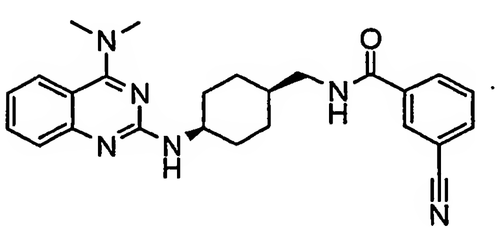
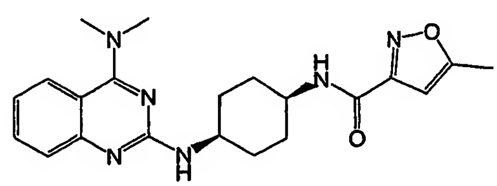
 ,  ,

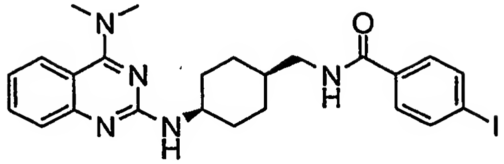
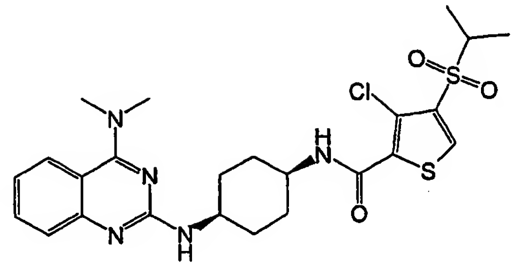
 ,  ,

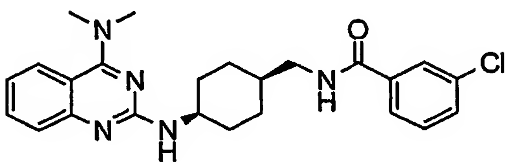
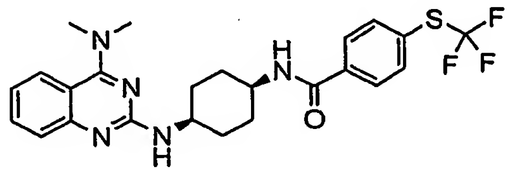
 ,  ,

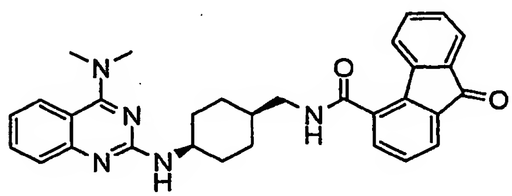
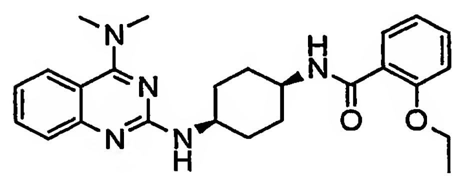
 ,  ,

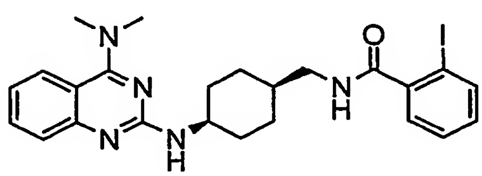
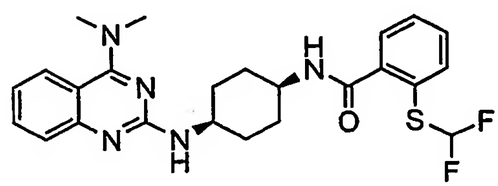
 ,  ,

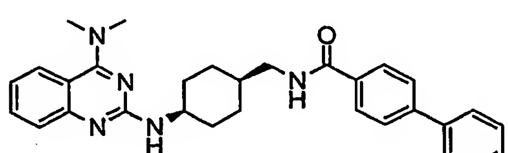
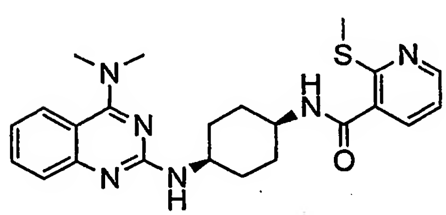
 ,  ,

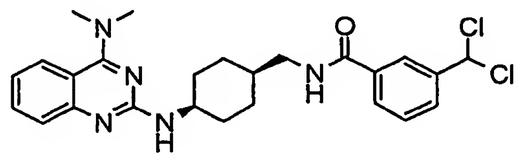
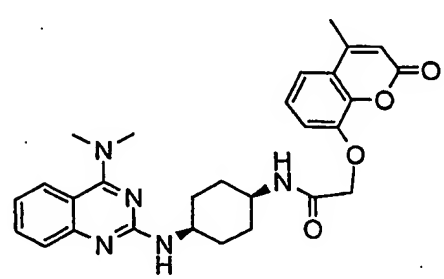
 ,  ,

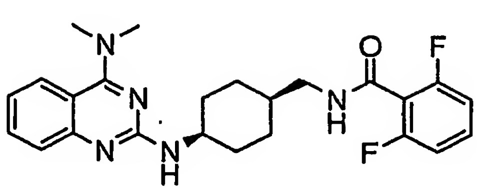
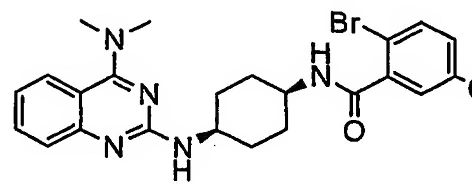
 ,  ,

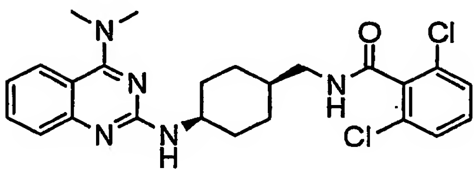
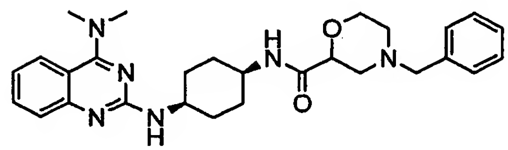
 ,  ,

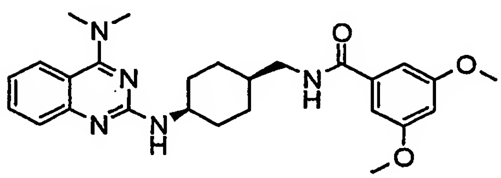
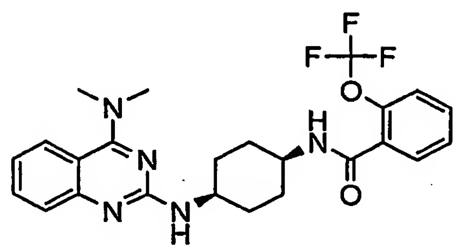
 ,  ,

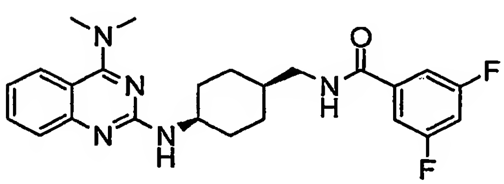
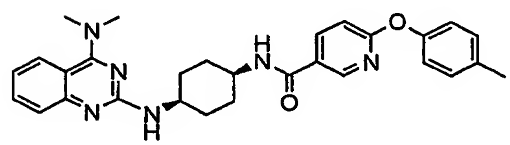
 ,  ,

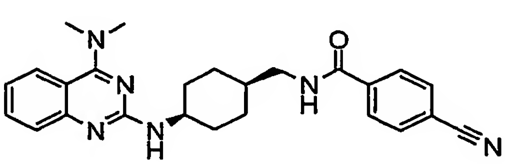
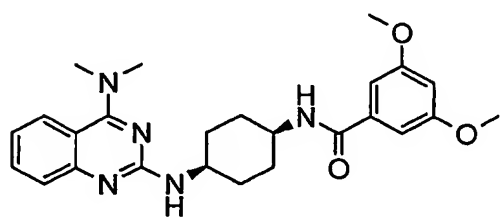
 ,  ,

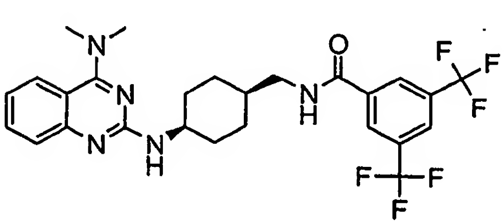
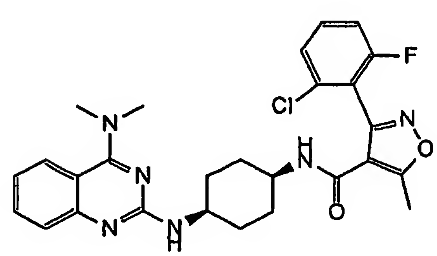
 ,  ,

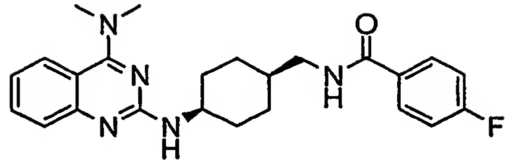
 ,  ,

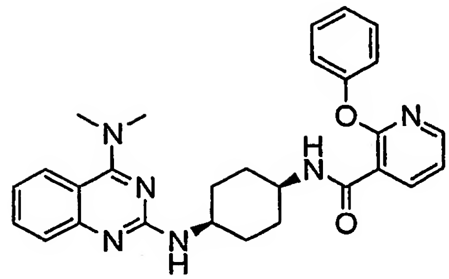
 ,  ,

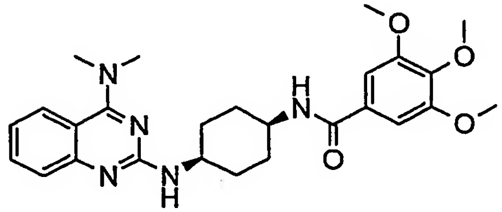
 ,  ,

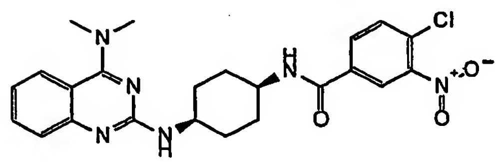
 ,  ,

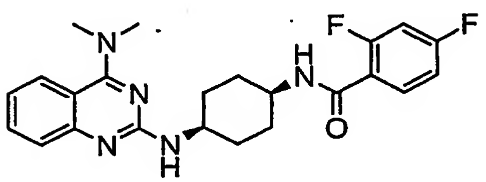
 ,  ,

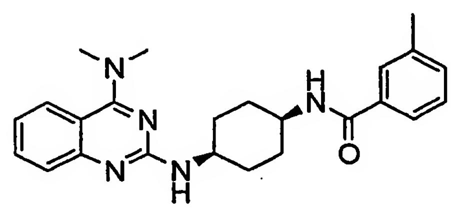
 ,

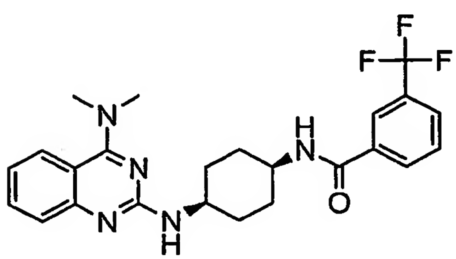
 ,

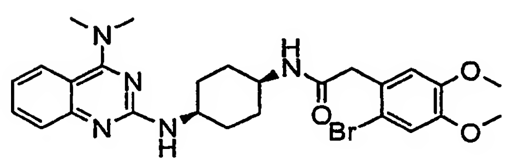
 ,

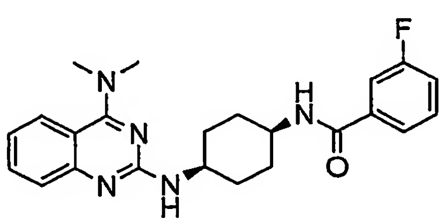
 ,

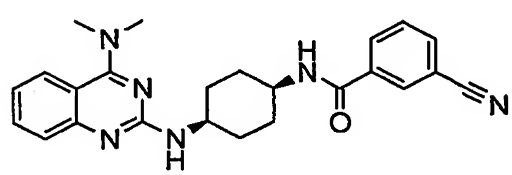
 ,

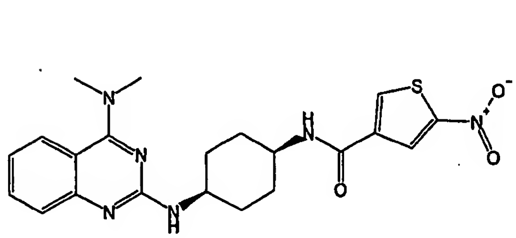
 ,

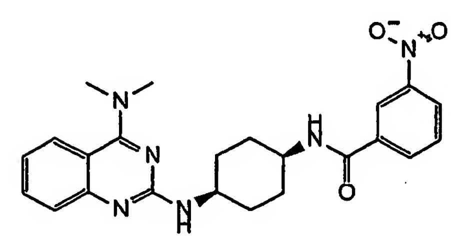
 ,

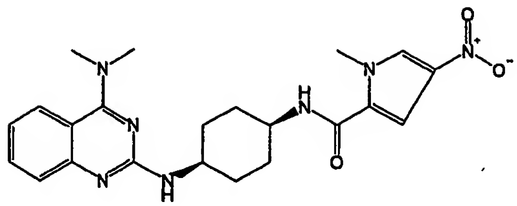
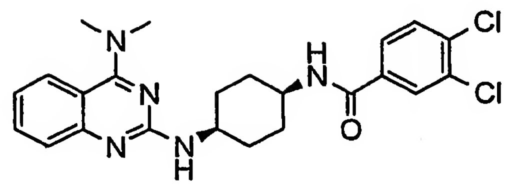
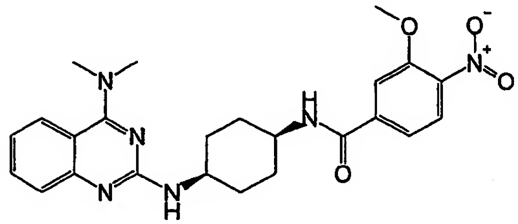
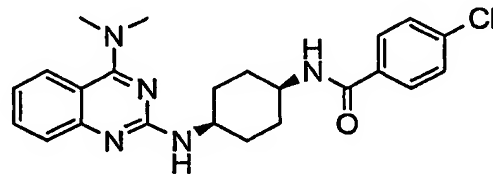
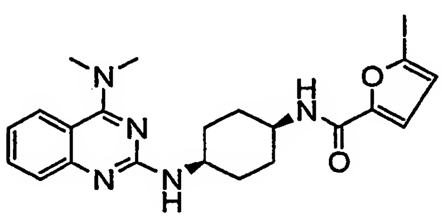
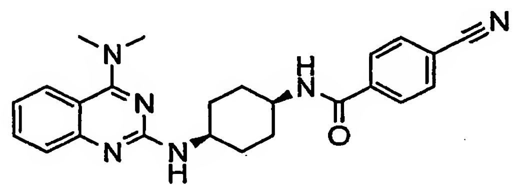
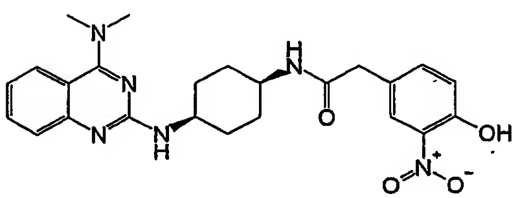
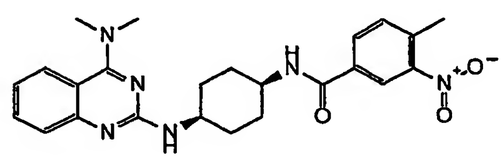
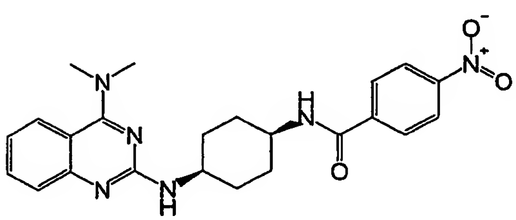
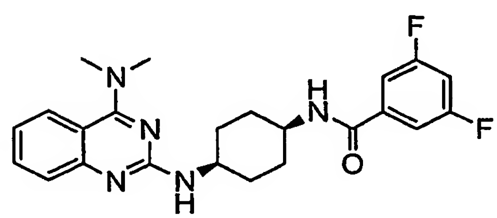
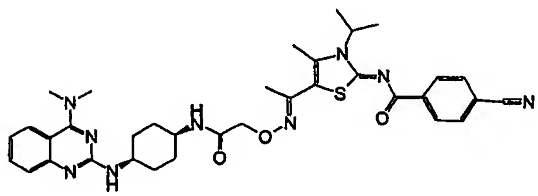
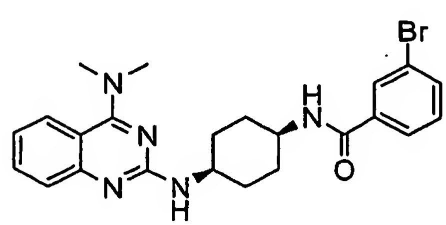
 ,

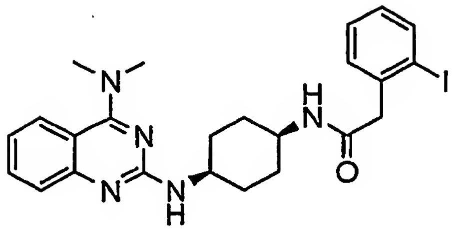
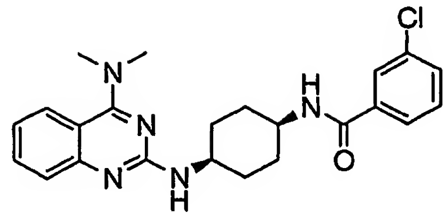
 ,

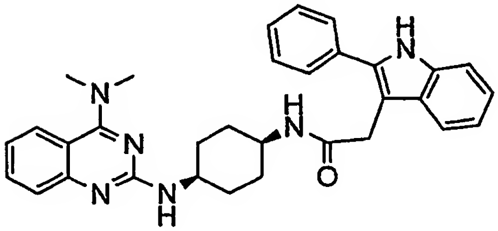
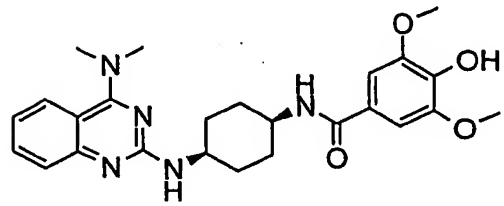
 ,

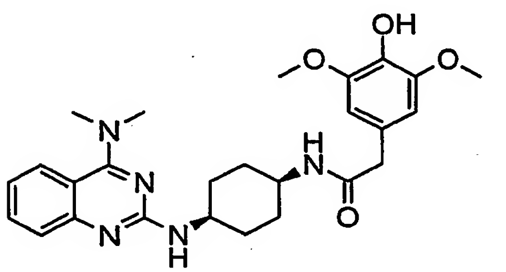
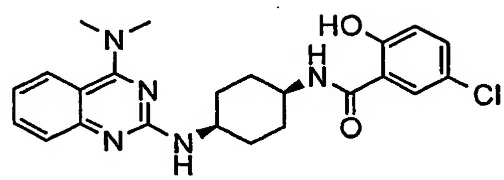
 ,

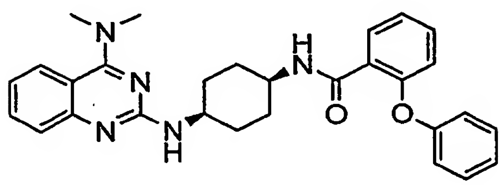
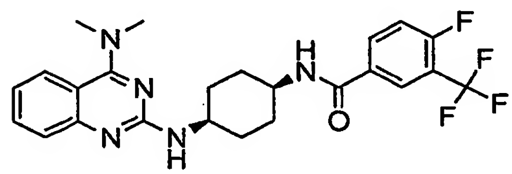
 ,

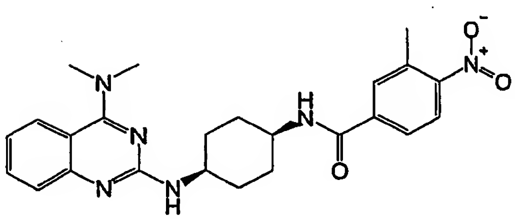
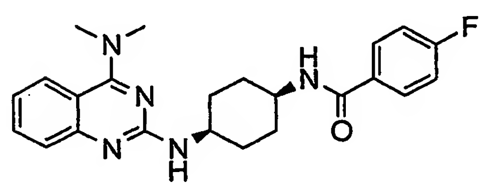

,

,

,

,

,

,

,

,

,

,

,

,

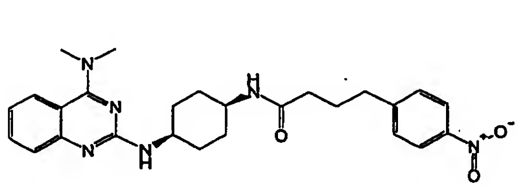
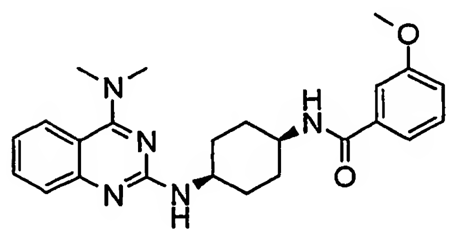
 ,  ,

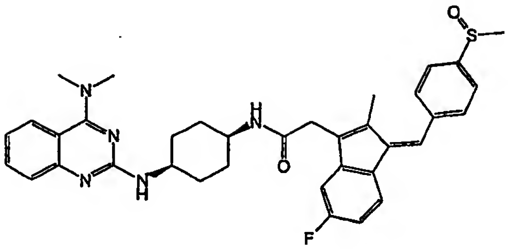
 ,  ,

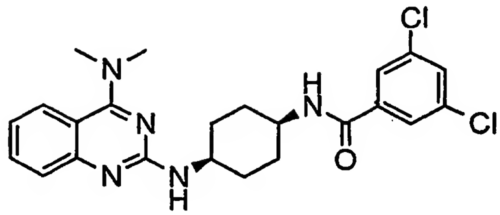
 ,  ,

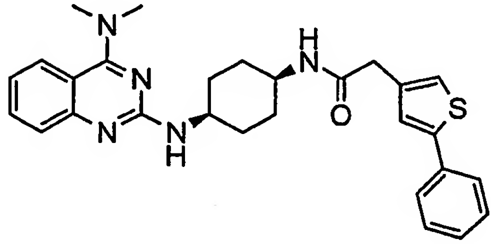
 ,  ,

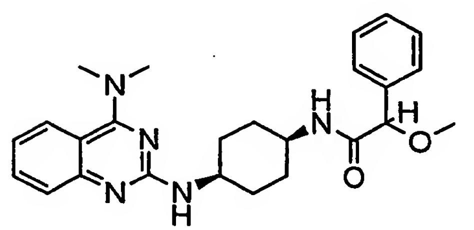
 ,  ,

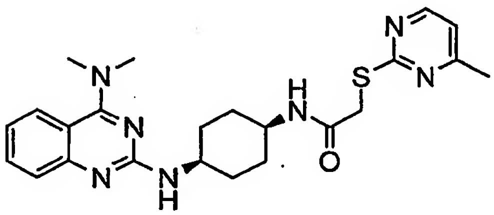
 ,  ,

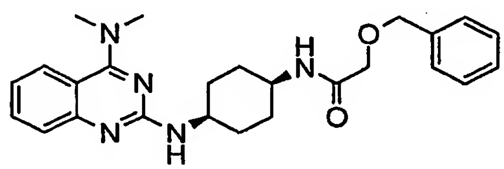
 ,

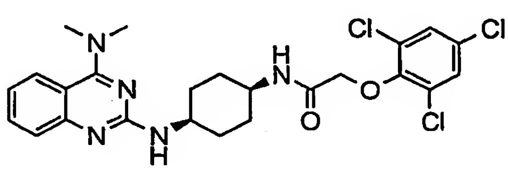
 ,

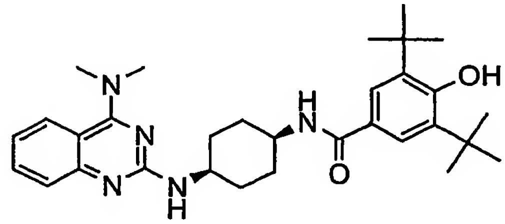
 ,

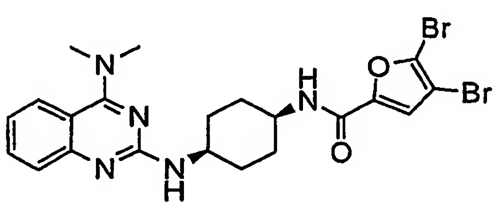
 ,

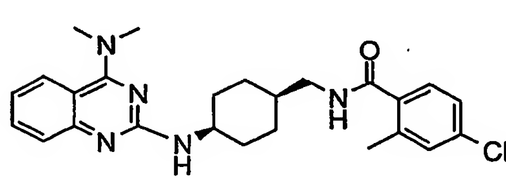
 ,

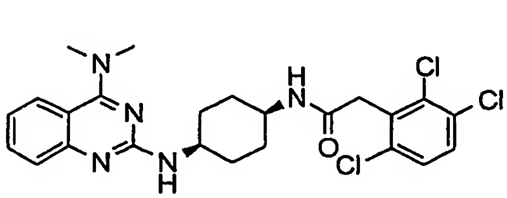
 ,

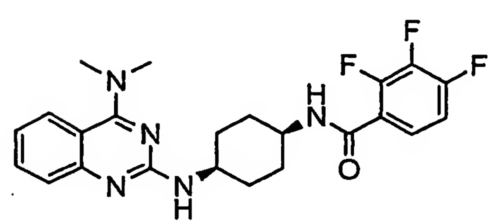
 ,

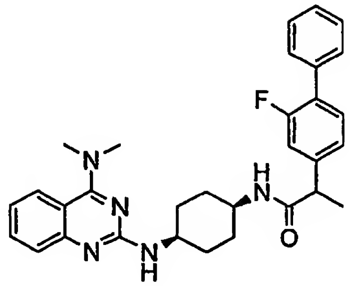
 ,

 ,

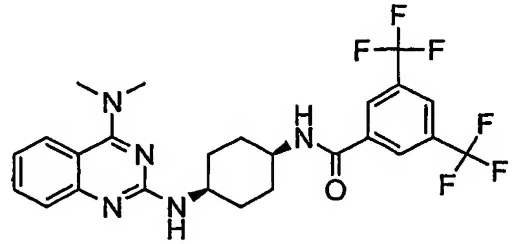
 ,

 ,

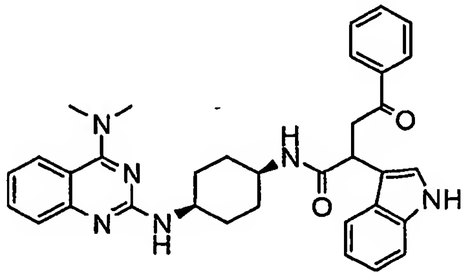
 ,



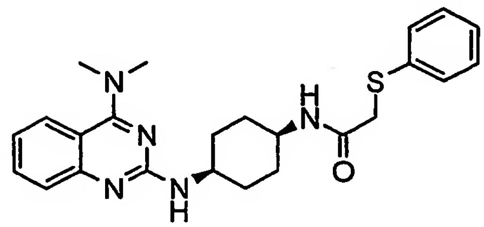
,



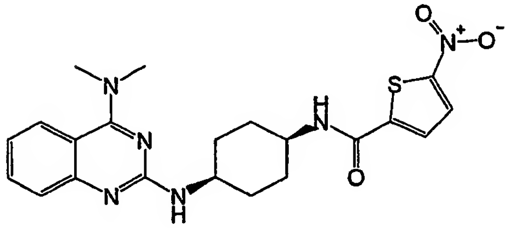
,



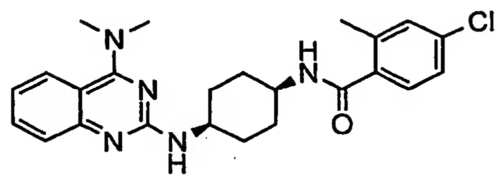
,



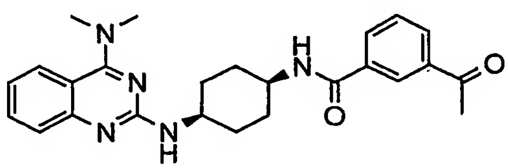
,



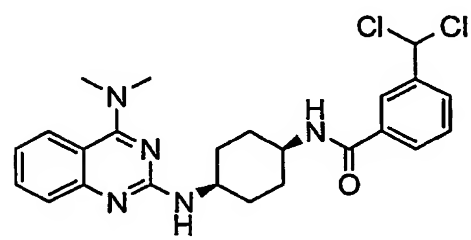
,



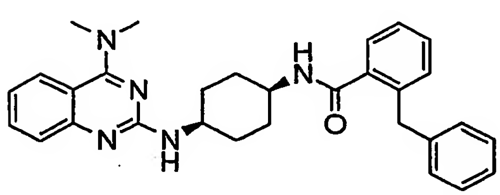
,



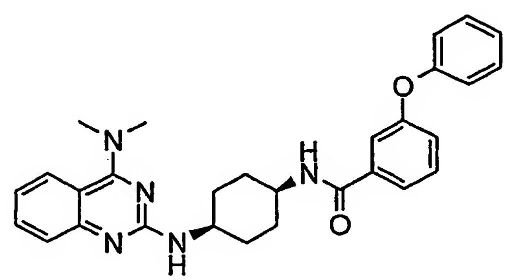
,



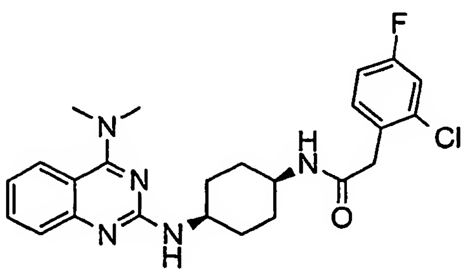
,



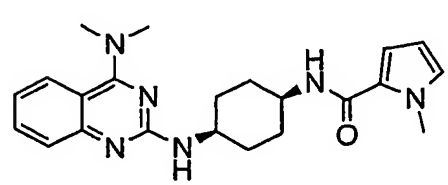
,



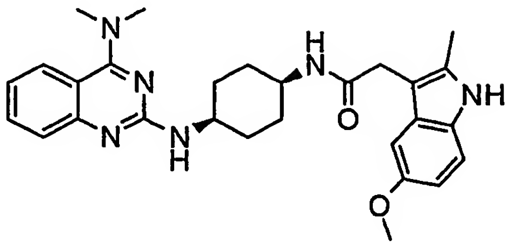
,

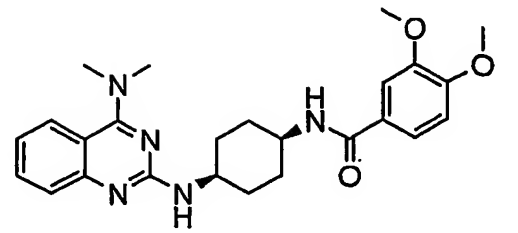


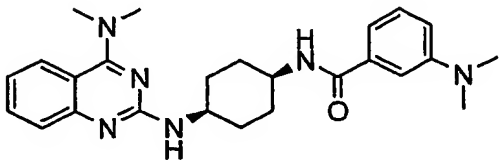
,

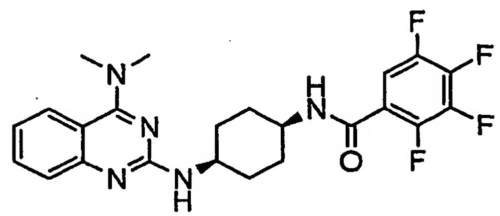


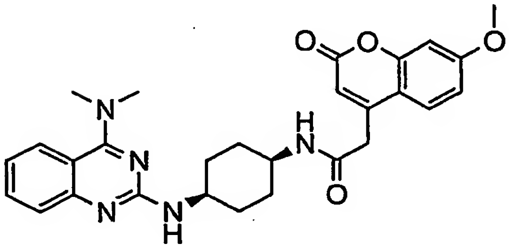
,

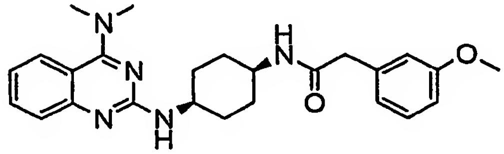
 ,

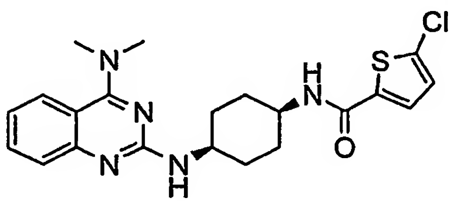
 ,

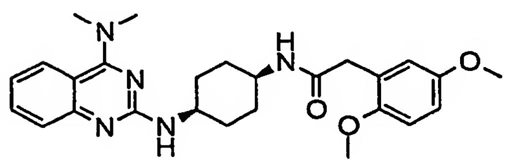
 ,

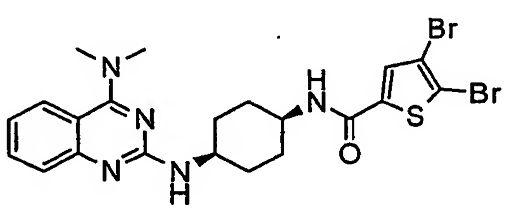
 ,

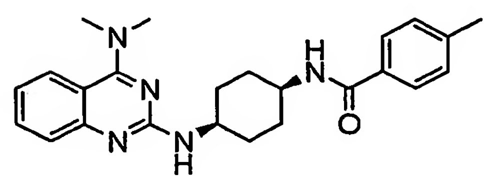
 ,

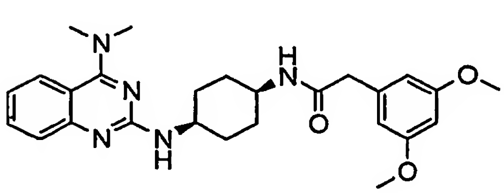
 ,

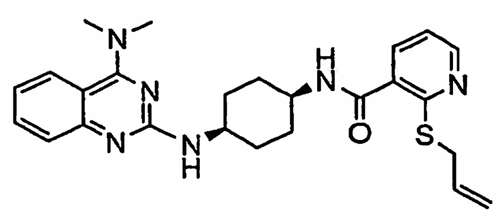
 ,

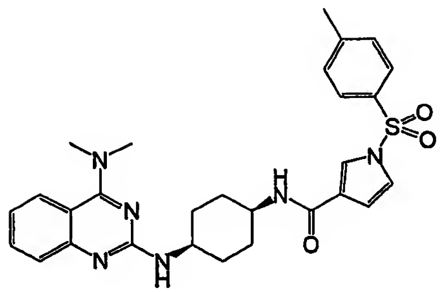
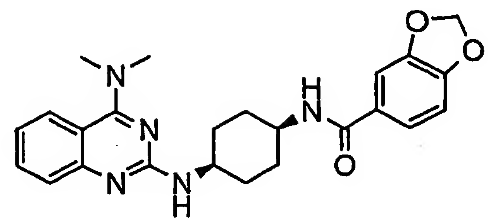
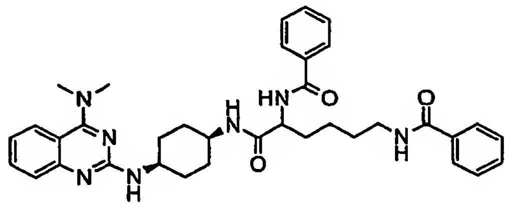
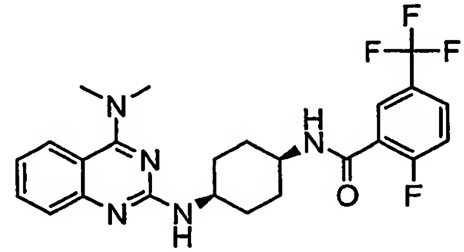
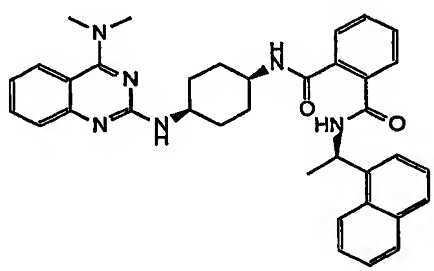
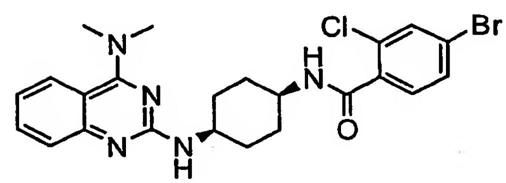
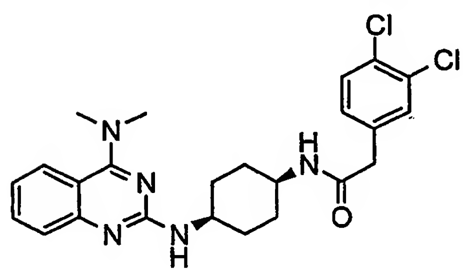
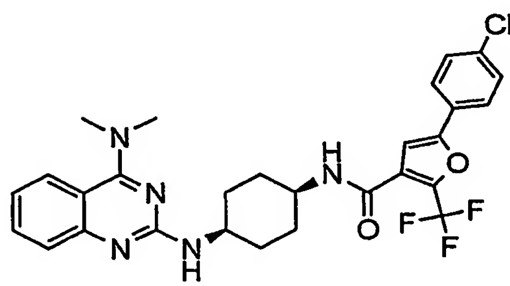
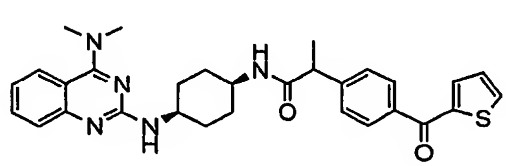
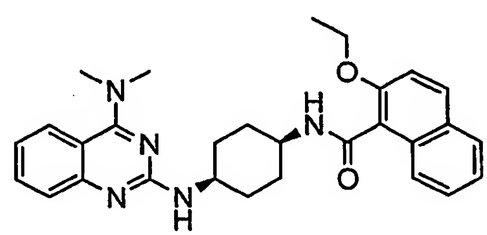
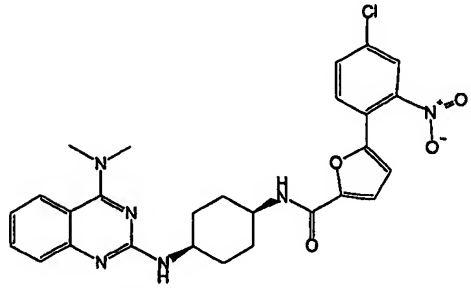
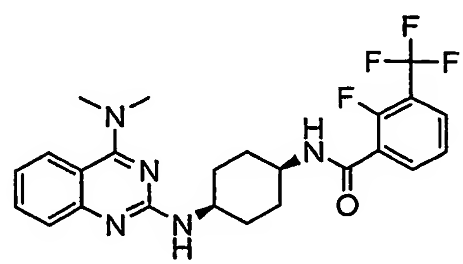
 ,

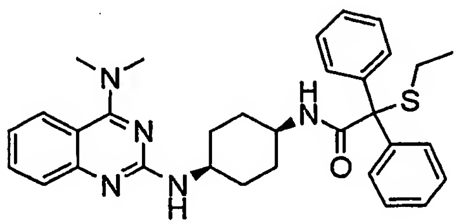
 ,

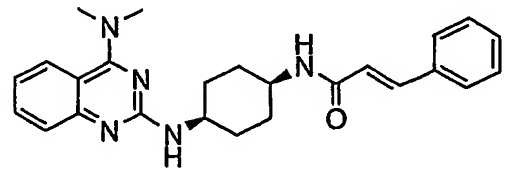
 ,

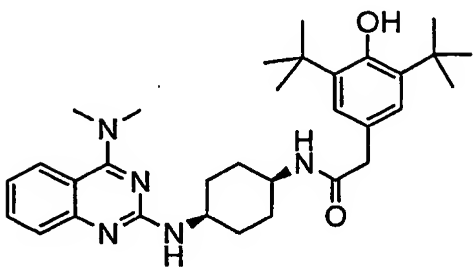
 ,

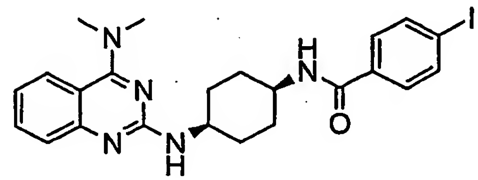
 ,

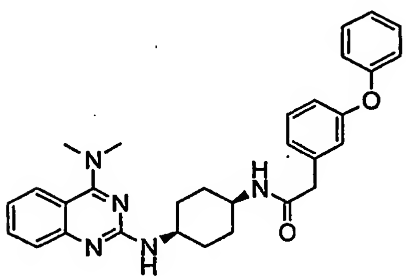

,

,

,

,

,

,

,

,

,

,

,

,

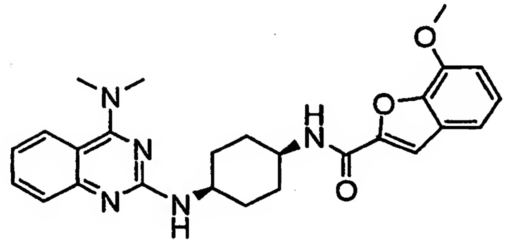
 ,

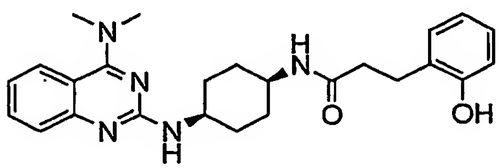
 ,

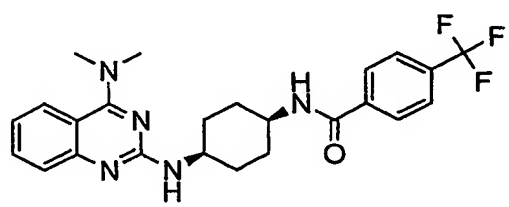
 ,

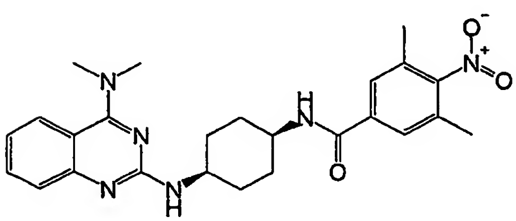
 ,

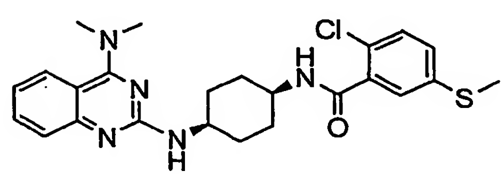
 ,

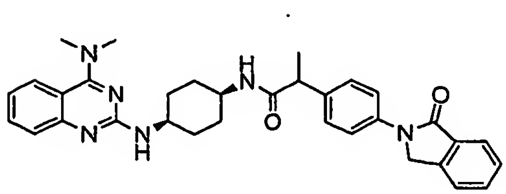
 ,

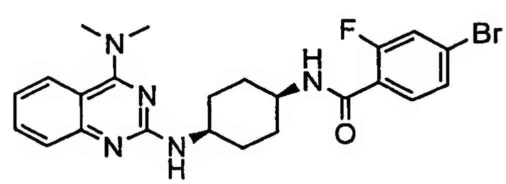
 ,

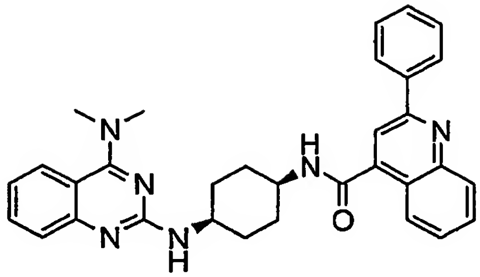
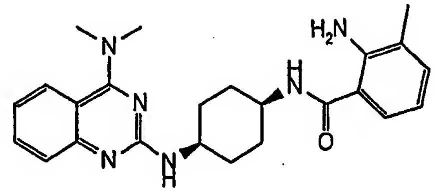
 ,

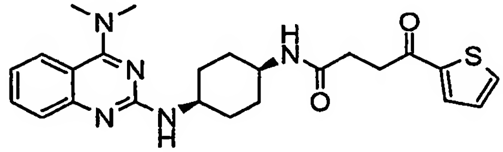
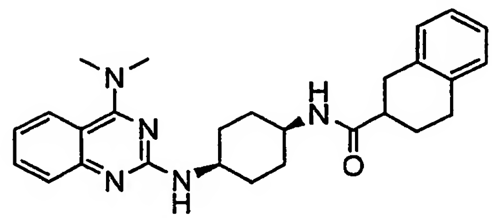
 ,

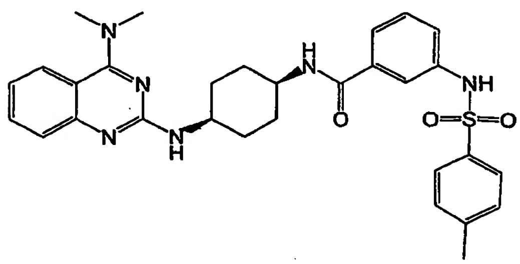
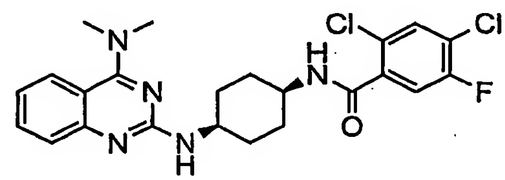
 ,

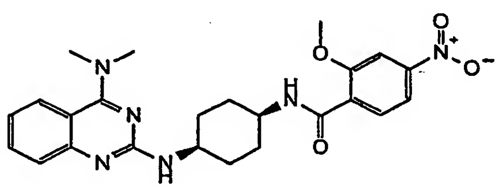
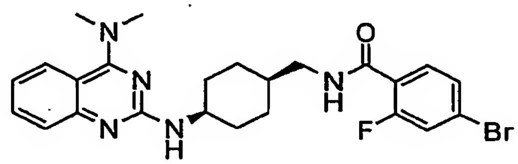
 ,

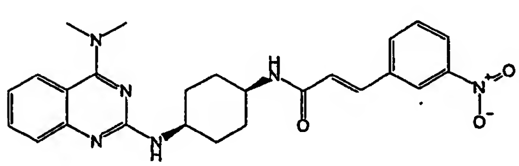
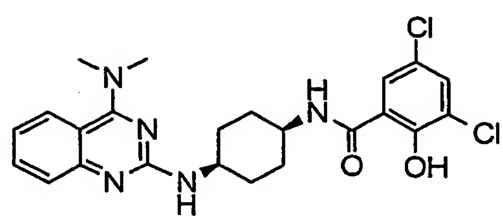
 ,

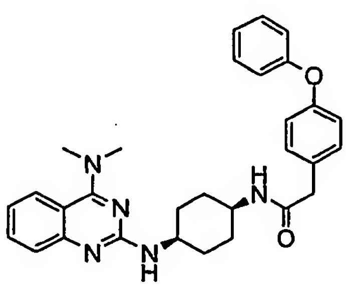
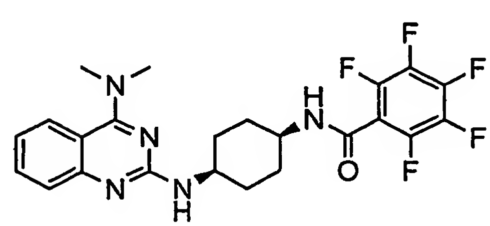
 ,  ,

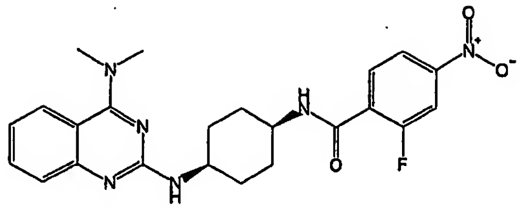
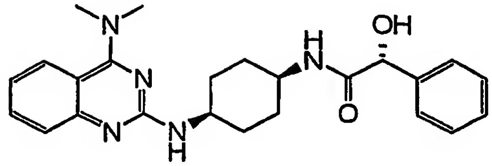
 ,  ,

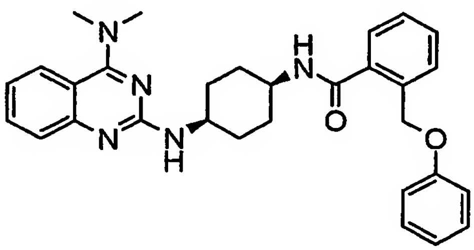
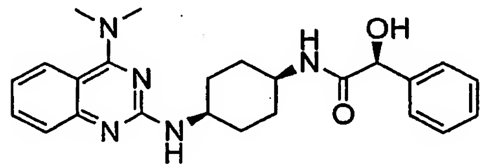
 ,  ,

 ,  ,

 ,  ,

 ,  ,

 ,  ,

 , and 

; or, in case of, a salt thereof.

Other more preferred compounds of this invention are those compounds of Formula I wherein,

Q is Formula II;

R_1 represents

(i) C_1-C_{10} alkyl,

C_1-C_{10} alkyl substituted by substituent(s) independently selected from

•C_5-C_6 cycloalkyl,

•carbocyclic aryl,

•heterocyclyl,

(ii) C_3-C_6 cycloalkyl,

(iii) carbocyclic aryl,

(iv) or heterocyclyl;

R_2 is methylamino or dimethylamino;

L is selected from Formula XX - XXII;

Y is -C(O)-;

wherein carbocyclic aryl is phenyl, naphthyl, anthranyl, or biphenyl;

heterocyclyl is 1,3-dioxo-isoindolyl, 1*H*-indolyl, 1-oxo-3*H*-isobenzofuranyl, 2,3-dihydro-benzo[1,4]dioxinyl, 3,4-dihydro-2*H*-benzo[b][1,4]dioxepinyl, 4-oxo-3,4-dihydro-phthalazinyl, 9,10,10-trioxo-thioxanthenyl, 9*H*-xanthenyl, benzimidazolyl, benzo[1,3]dioxolyl, benzo[2,1,3]oxadiazolyl, benzo[b]thienyl, furyl, imidazolyl, isoxazolyl, morpholino, oxolanyl, piperidyl, pyridyl, quinoxalyl, thienyl, quinolyl, or benzothiazolyl;

halogen is fluoro, chloro, bromo, or iodo.

Further other more preferred compounds of this invention are those compounds of Formula I wherein,

Q is Formula II;

R_1 represents

(i) C_1-C_4 alkyl,

C_1-C_4 alkyl substituted by substituent(s) independently selected from

•cyclopentyl,

•carbocyclic aryl,

•heterocyclyl,

(ii) carbocyclic aryl,

(iii) or heterocyclyl;

R_2 is methylamino or dimethylamino;

L is selected from Formula XX - XXII;

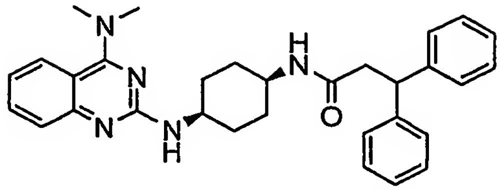
Y is -C(O)-;

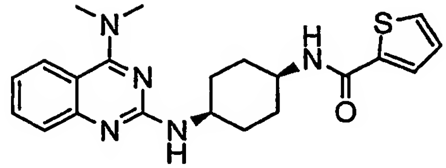
wherein carbocyclic aryl is phenyl, naphthyl, anthranyl, or biphenyl;

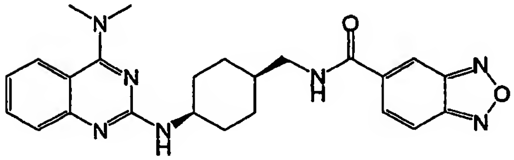
heterocyclyl is 9*H*-xanthenyl, benzo[1,3]dioxolyl, benzo[2,1,3]oxadiazolyl, benzo[b]thienyl, thienyl, 1*H*-indolyl, quinoxalyl, quinolyl, or benzothiazolyl;

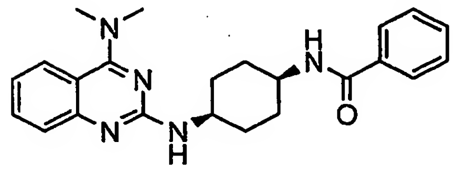
halogen is fluoro, chloro, bromo, or iodo.

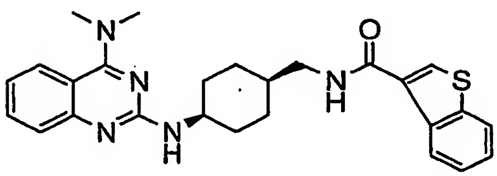
The following compounds are specially preffered;

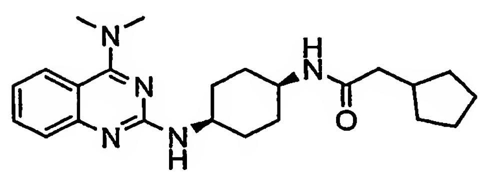
 ,

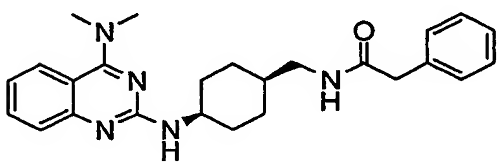
 ,

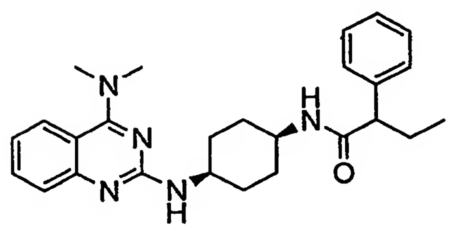
 ,

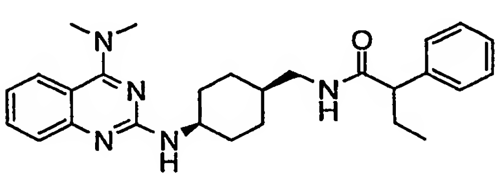
 ,

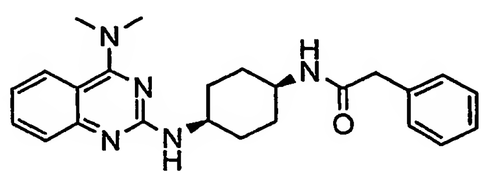
 ,

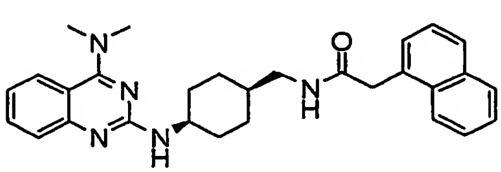
 ,

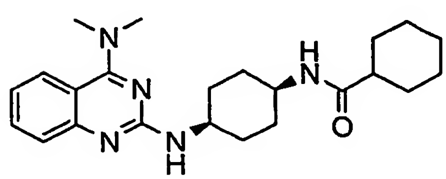
 ,

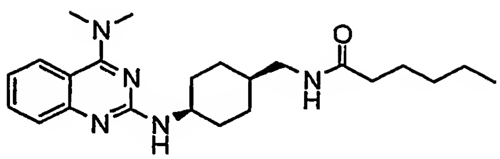
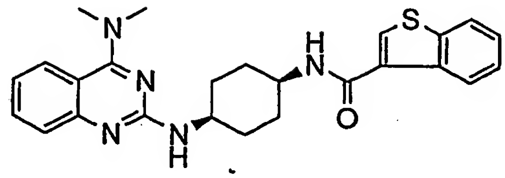
 ,

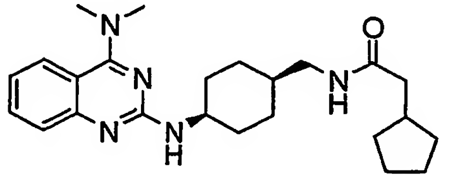
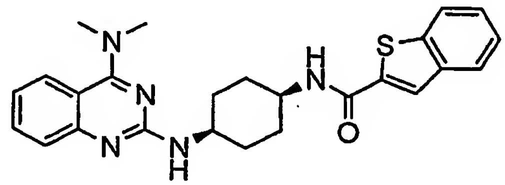
 ,

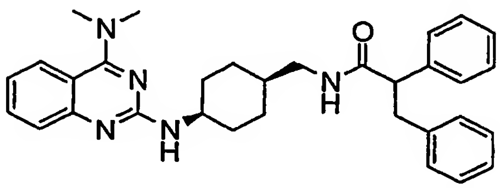
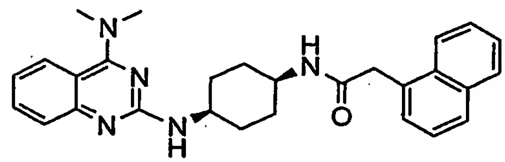
 ,

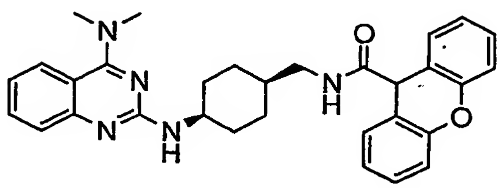
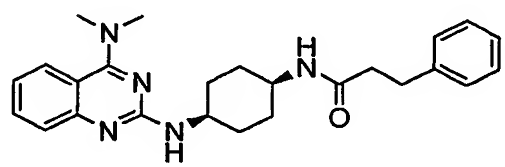
 ,

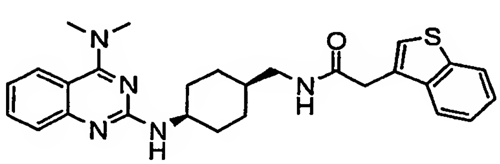
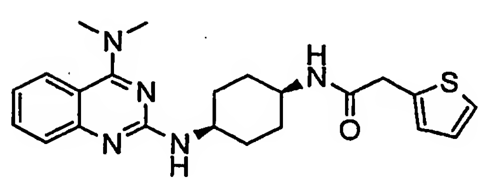
 ,

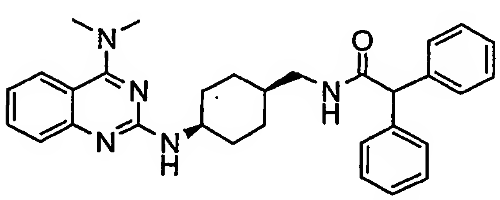
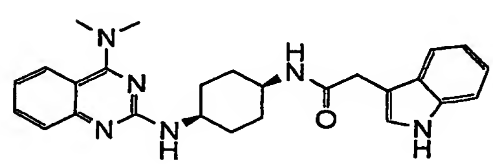
 ,  ,

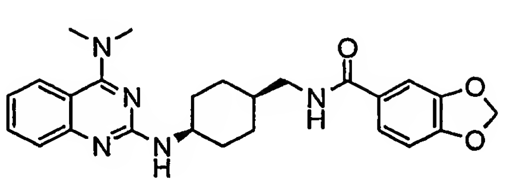
 ,  ,

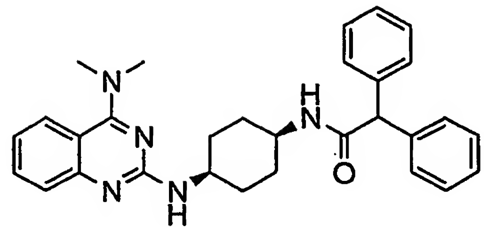
 ,  ,

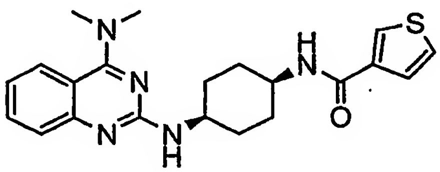
 ,  ,

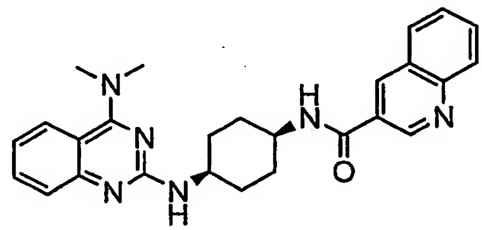
 ,  ,

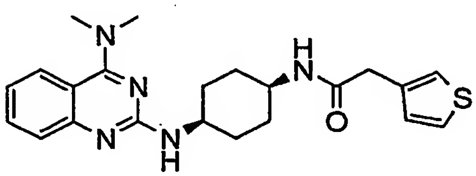
 ,  ,

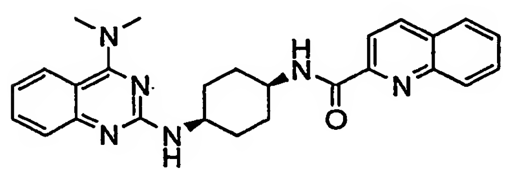
 ,

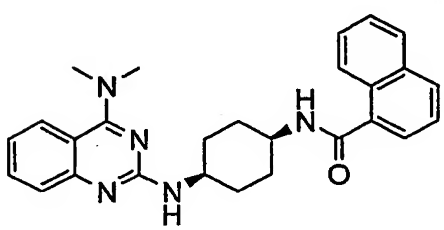
 ,

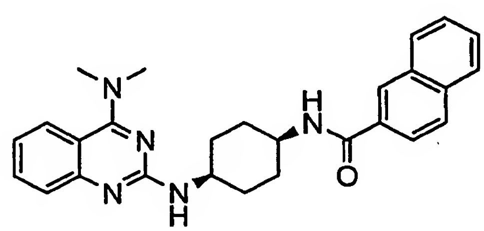
 ,

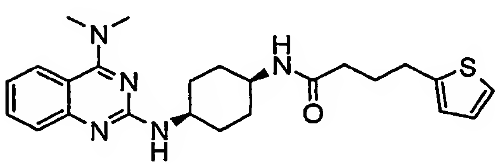
 ,

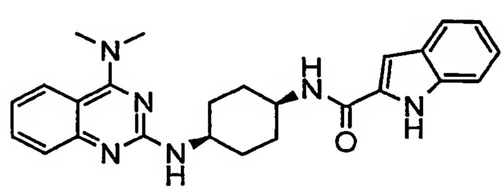
 ,

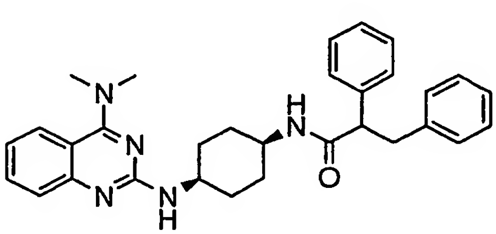
 ,

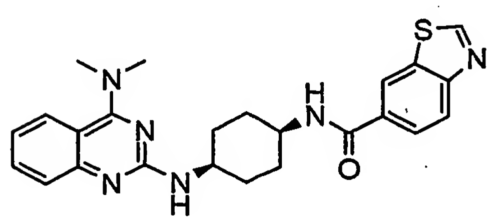
 ,

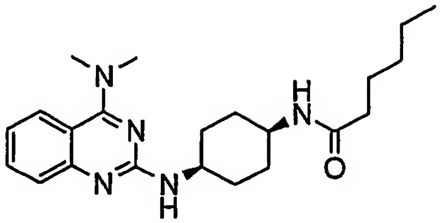
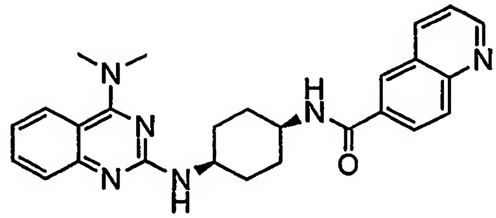
 ,

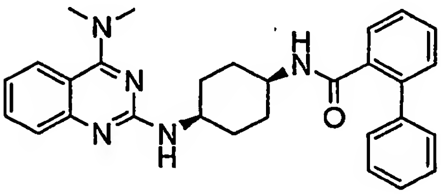
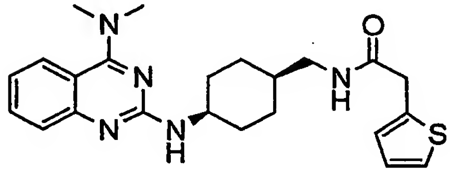
 ,

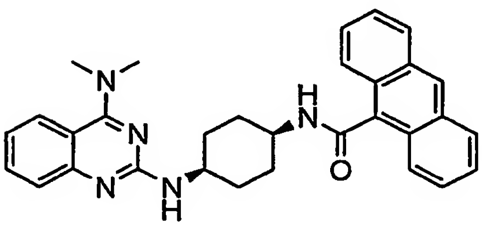
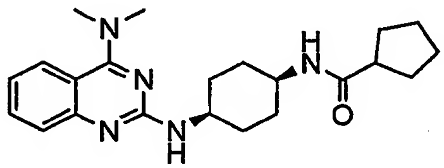
 ,

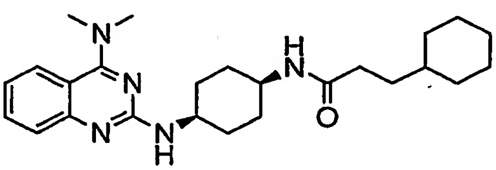
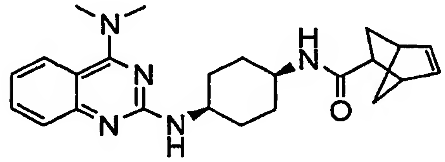
 ,

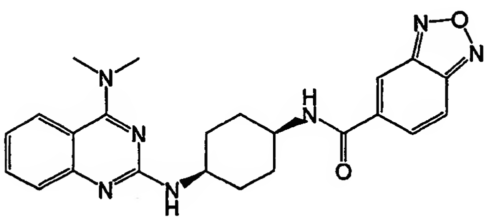
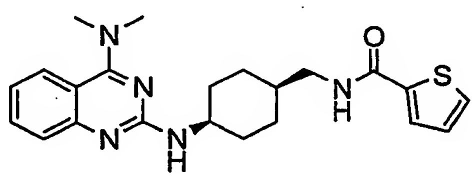
 ,

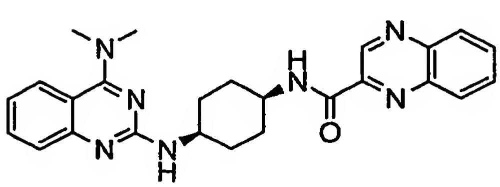
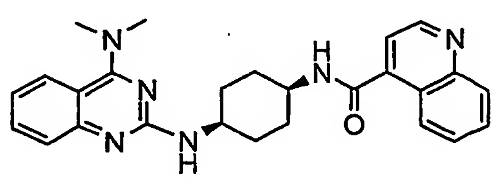
 ,  ,

 ,  ,

 ,  ,

 ,  ,

 ,  ,

 , and 

; or, in case of, a salt thereof.

Preferred compounds of this invention are those compounds of Formula I wherein,

Q is Formula II;

R_1 represents

(i) C_1-C_{10} alkyl,

C_1-C_{10} alkyl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•oxo,

•C_1-C_3 alkoxy,

•C_1-C_3 alkoxy substituted by substituent(s) independently selected from

••carbocyclic aryl,

••heterocyclyl,

••heterocyclyl substituted by C_1-C_3 alkyl,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by substituent(s) independently selected from

••halogen,

••nitro,

••carbocyclic aryl,

••carbocyclic aryl substituted by C_1-C_3 alkoxy,

••C_1-C_4 alkyl,

••C_1-C_4 alkyl substituted by substituent(s) independently selected from

•••mono- or di-C_1-C_3 alkylamino,

•••mono- or di-C_1-C_3 alkylamino substituted by carbocyclic aryl,

•••mono- or di-C_1-C_3 alkylamino substituted by halogenated carbocyclic aryl,

•mono- or di-C_1-C_3 alkylamino,

•mono- or di-C_1-C_3 alkylamino substituted by substituent(s) independently selected from

••cyano,

••carbocyclic aryl,

••heterocyclyl,

•mono- or di-carbocyclic arylamino,

•mono- or di-carbocyclic arylamino substituted by C_1-C_3 alkyl,

•C_1-C_3 alkylcalbonylamino,

•C_1-C_4 alkoxycalbonylamino,

•carbocyclic arylsulfonylamino,

•carbocyclic arylsulfonylamino substituted by substituent(s) independently selected from

••nitro,

••C_1-C_3 alkyl,

••mono- or di-C_1-C_3 alkylamino,

•C_1-C_3 alkylthio,

•C_1-C_3 alkylthio substituted by substituent(s) independently selected from

••mono- or di-carbocyclic arylamino,

••halogenated mono- or di-carbocyclic arylamino,

••carbocyclic aryl,

••carbocyclic aryl substituted by substituent(s) independently selected from

•••halogen,

•••C_1-C_3 alkoxy,

•carbocyclic arylthio,

•carbocyclic arylthio substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

•carbocyclic arylsulfonyl,

•halogenated carbocyclic arylsulfonyl,

•heterocyclylthio,

•C_3-C_6 cycloalkyl,

•C_3-C_6 cycloalkyl substituted by C_1-C_3 alkyl,

•carbocyclyl,

•carbocyclyl substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••C_2-C_3 alkenyl,

••C_2-C_3 alkenyl substituted by carbocyclic aryl,

••C_2-C_3 alkenyl substituted by carbocyclic aryl substituted C_1-C_3 alkylsulfinyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••nitro,

••C_1-C_4 alkyl,

••C_1-C_4 alkyl substituted by substituent(s) independently selected from

•••halogen,

•••hydroxy,

•••carbocyclic aryl,

•••mono- or di-carbocyclic arylamino,

•••mono- or di-carbocyclic arylamino substituted by substituent(s) independently selected from

••••halogen,

••••nitro,

••••C_1-C_3 alkyl,

••••C_1-C_3 alkoxy,

••••halogenated C_1-C_3 alkoxy,

••C_1-C_3 alkoxy,

••C_1-C_3 alkoxy substituted by substituent(s) independently selected from

•••halogen,

•••carbocyclic aryl,

••carbocyclic aryloxy,

••C_1-C_3 alkoxycarbonyl,

••mono- or di-C_1-C_3 alkylamino,

••C_1-C_3 alkylthio,

••halogenated C_1-C_3 alkylthio,

••C_1-C_3 alkylsulfonyl,

••C_3-C_6 cycloalkyl,

••carbocyclic aryl,

••heterocyclyl,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••C_1-C_3 alkoxy substituted by carbocyclic aryl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

(ii) C_2-C_8 alkenyl,

C_2-C_8 alkenyl substituted by substituent(s) independently selected from

•halogen,

•C_1-C_3 alkoxy,

•C_1-C_3 alkoxy substituted by carbocyclic aryl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••C_1-C_3 alkoxy,

••halogenated C_1-C_3 alkoxy,

•heterocyclyl,

•heterocyclyl substituted by nitro,

(iii) C_2-C_4 alkynyl,

C_2-C_4 alkynyl substituted by carbocyclic aryl,

(iv) C_3-C_6 cycloalkyl,

C_3-C_6 cycloalkyl substituted by substituent(s) independently selected from

•C_1-C_3 alkyl,

•C_1-C_3 alkyl substituted by substituent(s) independently selected from

••hydroxy,

••oxo,

••carbocyclic aryl,

•mono- or di-C_1-C_3 alkylamino,

•mono- or di-C_1-C_3 alkylamino substituted by carbocyclic aryl,

•carbocyclic aryl,

(v) C_3-C_6 cycloalkeyl,

C_3-C_6 cycloalkeyl substituted by C_1-C_3 alkyl,

(vi) carbocyclyl,

carbocyclyl substituted by substituent(s) independently selected from

•hydroxy,

•nitro,

(vii) carbocyclic aryl,

carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•cyano,

•nitro,

•C_1-C_9 alkyl,

•C_1-C_9 alkyl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••oxo,

••C_1-C_3 alkoxy,

••carbocyclic aryloxy,

••mono- or di-C_1-C_3 alkylamino-N-oxy,

••mono- or di-C_1-C_3 alkylamino,

••mono- or di-C_1-C_3 alkylamino substituted by carbocyclic aryl,

••mono- or di-carbocyclic arylamino,

••mono- or di-carbocyclic arylamino substituted by C_1-C_3 alkoxy,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

••heterocyclyl,

••heterocyclyl substituted by C_1-C_3 alkyl,

•C_2-C_3 alkenyl,

•C_2-C_3 alkenyl substituted by carbocyclic aryl,

•C_1-C_9 alkoxy,

•C_1-C_9 alkoxy substituted by substituent(s) independently selected from

••hydroxy,

••halogen,

••carboxy,

••mono- or di-C_1-C_3 alkylamino,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

••heterocyclyl,

••heterocyclyl substituted by substituent(s) independently selected from

•••heterocyclyl,

•••heterocyclyl substituted by substituent(s) independently selected from

••••halogen,

••••C_1-C_3 alkyl,

••••halogenated C_1-C_3 alkyl,

•C_2-C_3 alkenyloxy,

•C_1-C_3 alkylcarbonyloxy,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by substituent(s) independently selected from

••halogen,

••C_1-C_4 alkyl,

••halogenated C_1-C_4 alkyl,

••C_1-C_3 alkoxy,

•heterocyclyloxy,

•heterocyclyloxy substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl,

•(carbocyclic aryl)$S(O)_2O$,

•carboxy,

•C_1-C_3 alkoxycarbonyl,

•mono- or di-C_1-C_3 alkylaminocarbonyl,

•mono- or di-C_1-C_3 alkylaminocarbonyl substituted by carbocyclic aryl,

•amino,

•mono- or di-C_1-C_4 alkylamino,

•mono- or di-C_1-C_4 alkylamino substituted by cyano,

•mono- or di-carbocyclic arylamino,

•C_1-C_3 alkylcarbonylamino,

•carbocyclic arylsulfonylamino,

•carbocyclic arylsulfonylamino substituted by C_1-C_3 alkyl,

•(carbocyclic aryl)NHC(O)NH,

•(carbocyclic aryl)NHC(O)NH substituted by C_1-C_3 alkoxy,

•(carbocyclic aryl)NHC(O)NH substituted by haloganated C_1-C_3 alkoxy,

•C_1-C_3 alkylthio,

•halogenated C_1-C_3 alkylthio,

•carbocyclic arylthio,

•halogenated carbocyclic arylthio,

•carbocyclic arylthio substituted by C_1-C_3 alkyl,

•heterocyclylthio,

•C_1-C_3 alkylsulfonyl,

•mono- or di-C_1-C_3 alkylaminosulfonyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••C_1-C_7 alkyl,

••halogenated C_1-C_7 alkyl,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••C_1-C_3 alkyl,

••carbocyclic aryl,

••halogenated carbocyclic aryl,

(viii) heterocyclyl,

or heterocyclyl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•cyano,

•nitro,

•C_1-C_4 alkyl,

•C_1-C_4 alkyl substituted by substituent(s) independently selected from

••halogen,

••hydroxy,

••oxo,

••C_1-C_3 alkylcarbonyloxy,

••C_1-C_3 alkoxycarbonyl,

••C_1-C_3 alkylthio,

••C_1-C_3 alkylthio substituted by carbocyclic aryl,

••C_1-C_3 alkylthio substituted by halogenated carbocyclic aryl,

••carbocyclic aryl,

••carbocyclic aryl substituted by substituent(s) independently selected from

•••halogen,

•••nitro,

••heterocyclyl,

•C_1-C_3 alkoxy,

•C_1-C_3 alkoxy substituted by carbocyclic aryl,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by C_1-C_3 alkyl,

•mono- or di-C_1-C_3 alkylamino,

•C_1-C_4 alkylcarbonylamino,

•C_1-C_3 alkylthio,

•carbocyclic arylthio,

•halogenated carbocyclic arylthio,

•carbocyclic arylthio substituted by C_1-C_3 alkoxycarbonyl,

•heterocyclylthio,

•heterocyclylthio substituted by C_1-C_3 alkyl,

•C_1-C_3 alkylsulfonyl,

•carbocyclic arylsulfonyl,

•carbocyclic arylsulfonyl substituted by C_1-C_4 alkyl,

•C_1-C_3 alkoxycarbonyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••nitro,

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••halogenated C_1-C_3 alkoxy,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••C_1-C_3 alkoxycarbonyl;

R_2 is -$NHNH_2$, -NHNHBoc, -N(R_{2a})(R_{2b}), morpholino, 4-acetyl-piperazyl, or 4-phenyl-piperazyl;

wherein R_{2a} is H or C_1-C_3 alkyl;

R_{2b} is C_1-C_4 alkyl, C_1-C_4 alkyl substituted by substituent(s) independently selected from

•hydroxy,

•C_1-C_3 alkoxy,

•amino,

•-NHBoc,

•C_3-C_6 cycloalkyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••-SO_2NH_2,

•heterocyclyl,

C_3-C_6 cycloalkyl, carbocyclic aryl, carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•C_1-C_3 alkyl,

•C_1-C_3 alkoxy,

or a group of Formula IV;

wherein Boc is carbamic acid *tert*-butyl ester and R_3 is C_1-C_3 alkyl or C_1-C_3 alkyl substituted by substituent(s) independently selected from

•carbocyclic aryl,

•halogenated carbocyclic aryl,

•carbocyclic aryl substituted by C_1-C_3 alkoxy;

L is selected from Formula V - XIX;

wherein R_4 is H or C_1-C_3 alkyl;

R_5 is H, C_1-C_3 alkyl, or C_1-C_3 alkyl substituted by a substituted carbocyclic aryl;

Y is $-(CH_2)_m$, m is 0 or 1;

wherein carbocyclic aryl is phenyl, naphthyl, phenanthryl, or biphenyl;

carbocyclyl is 9*H*-fluorenyl, 9-oxo-fluorenyl, acenaphthyl, anthraquinonyl, indanyl, or indenyl;

heterocyclyl is 1,2,3-thiadiazolyl, 1,2,3-triazolyl, 1,2-dihydro-3-oxo-pyrazolyl, 1,3,4-thiadiazolyl, 1,3-dioxo-isoindolyl, 1,3-dioxolanyl, 1*H*-indolyl, 1*H*-pyrrolo[2,3-c]pyridyl, 1*H*-pyrrolyl, 2,2',5',2"-terthiophenyl, 2,2'-bithiophenyl, 2,3-dihydro-1-oxo-isoindolyl, 2,3-dihydro-benzo[1,4]dioxinyl, 2,3-dihydro-benzofuryl, 2,4-dihydro-3-oxo-pyrazolyl, 2*H*-benzopyranyl, 2-oxo-pyrrolidinyl, 3,4-dihydro-2*H*-benzo[1,4]oxazinyl, 3,4-dihydro-2*H*-benzo[b][1,4]dioxepinyl, 4*H*-benzo[1,3]dioxinyl, 4*H*-benzopyranyl, 4-oxo-1,5,6,7-tetrahydro-indolyl, 4-oxo-benzopyranyl, 9*H*-carbazolyl, 9*H*-xanthenyl, azetidinyl, benzimidazolyl, benzo[1,3]dioxolyl, benzo[b]thienyl, benzofuryl, benzothiazolyl, furyl, imidazo[2,1-b]thiazolyl, imidazolyl, isoxazolyl, morpholino, morpholinyl, oxolanyl, piperazyl, piperidyl, pyrazolo[5,1-b]thiazolyl, pyrazolyl, pyridyl, pyrimidyl, pyrrolidyl, quinolyl, quinoxalyl, thiazolidyl, thiazolyl, thienyl, or thiolanyl;

halogen is fluoro, chloro, bromo, or iodo.

Other preferred compounds of this invention are those compounds of Formula I wherein,

Q is Formula II;

R_1 represents

(i) C_1-C_{10} alkyl substituted by substituent(s) independently selected from

•methoxy,

•methoxy substituted by carbocyclic aryl,

•carbocyclic aryloxy,

•halogenated carbocyclic aryloxy,

•mono-C_1-C_2 alkylamino substituted by cyano,

•mono- or di-C_1-C_2 alkylamino substituted by carbocyclic aryl,

•mono-carbocyclic arylamino,

•mono-carbocyclic arylamino substituted by methyl,

•carbocyclic arylsulfonylamino substituted by methyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••nitro,

••C_1-C_4 alkyl,

••C_1-C_4 alkyl substituted by carboeyclic aryl,

••C_1-C_4 alkyl substituted by hydroxy,

••C_1-C_2 alkoxy,

••halogenated C_1-C_2 alkoxy,

•heterocyclyl substituted by carbocyclic aryl,

(ii) C_2-C_8 alkenyl substituted by substituent(s) independently selected from

•methoxy substituted by carbocyclic aryl,

•carbocyclic aryl,

•carbocyclic aryl substituted by methoxy,

(iii) C_2-C_4 alkynyl substituted by carbocyclic aryl,

(iv) cyclohexyl substituted by carbocyclic arylmethyl,

(v) carbocyclyl,

(vi) carbocyclic aryl,

carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•hydroxy,

•cyano,

•amino,

•C_1-C_9 alkyl,

•halogenated C_1-C_9 alkyl,

•C_1-C_9 alkoxy,

•C_1-C_9 alkoxy substituted by substituent(s) independently selected from

••halogen,

••halogenated carbocyclic aryl,

•propenyloxy,

•methylamino,

•di-C_1-C_2 alkylamino,

•di-C_1-C_2 alkylamino substituted by cyano,

•methylthio,

•halogenated methylthio,

(vii) heterocyclyl,

or heterocyclyl substituted by substituent(s) independently selected from

•halogen,

•C_1-C_4 alkyl,

•C_1-C_4 alkyl substituted by hydroxy,

•C_1-C_4 alkyl substituted by carbocyclic aryl,

•methoxy,

•C_1-C_2 alkoxycarbonyl,

•carbocyclic arylthio substituted by methoxycarbonyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••halogenated methyl,

•heterocyclyl;

R_2 is methylamino or dimethylamino;

L is selected from Formula Va, VIIIa, or IXa;

wherein R_4 and R_5 are independently selected from H or C_1-C_3 alkyl;

Y is -$(CH_2)_m$, m is 0 or 1;

wherein carbocyclic aryl is phenyl, naphthyl, phenanthryl, or biphenyl;

carbocyclyl is 9*H*-fluorenyl, acenaphthyl, or anthraquinonyl;

heterocyclyl is 1,2,3-thiadiazolyl, 1,2,3-triazolyl, 1,2-dihydro-3-oxo-pyrazolyl, 1,3-dioxolanyl, 1*H*-indolyl, 1*H*-pyrrolyl, 2,2',5',2''-terthiophenyl, 2,2'-bithiophenyl, 2,3-

dihydro-benzo[1,4]dioxinyl, 3,4-dihydro-2*H*-benzo[1,4]oxazinyl, 4-oxo-benzopyranyl, 9*H*-carbazolyl, 9*H*-xanthenyl, benzimidazolyl, benzo[1,3]dioxolyl, benzo[b]thienyl, benzofuryl, benzothiazolyl, furyl, imidazolyl, isoxazolyl, oxolanyl, pyrazolo[5,1-b]thiazolyl, pyrazolyl, pyridyl, pyrimidyl, quinolyl, quinoxalyl, thiazolidyl, thiazolyl, thienyl, 2*H*-benzopyranyl, 4*H*-benzo[1,3]dioxinyl, azetidinyl, imidazo[2,1-b]thiazolyl, morpholinyl, or 2,3-dihydro-benzofuryl;

halogen is fluoro, chloro, bromo, or iodo.

Other more preferred compounds of this invention are those compounds of Formula I wherein,

Q is Formula II;

R_1 represents

(i) C_1-C_7 alkyl substituted by substituent(s) independently selected from

•methoxy,

•methoxy substituted by carbocyclic aryl,

•carbocyclic aryloxy,

•halogenated carbocyclic aryloxy,

•mono-ethylamino substituted by cyano,

•di-methylamino substituted by carbocyclic aryl,

•mono-carbocyclic arylamino,

•mono-carbocyclic arylamino substituted by methyl,

•carbocyclic arylsulfonylamino substituted by methyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••nitro,

••C_1-C_4 alkyl,

••C_1-C_4 alkyl substituted by carbocyclic aryl,

••C_1-C_4 alkyl substituted by hydroxy,

••metoxy,

••halogenated methoxy,

•heterocyclyl substituted by carbocyclic aryl,

(ii) C_2-C_7 alkenyl substituted by substituent(s) independently selected from
•methoxy substituted by carbocyclic aryl,
•carbocyclic aryl,
•carbocyclic aryl substituted by methoxy,
(iii) butynyl substituted by carbocyclic aryl,
(iv) cyclohexyl substituted by carbocyclic arylmethyl,
(v) carbocyclyl,
(vi) carbocyclic aryl,
carbocyclic aryl substituted by substituent(s) independently selected from
•halogen,
•hydroxy,
•cyano,
•amino,
•C_1-C_2 alkyl,
•halogenated methyl,
•C_1-C_3 alkoxy,
•C_1-C_3 alkoxy substituted by substituent(s) independently selected from
••halogen,
••halogenated carbocyclic aryl,
•propenyloxy,
•di-C_1-C_2 alkylamino,
•di-C_1-C_2 alkylamino substituted by cyano,
•methylthio,
•halogenated methylthio,
(vii) heterocyclyl,
or heterocyclyl substituted by substituent(s) independently selected from
•halogen,
•C_1-C_3 alkyl,
•C_1-C_3 alkyl substituted by hydroxy,
•C_1-C_3 alkyl substituted by carbocyclic aryl,
•methoxy,
•ethoxycarbonyl,

•carbocyclic arylthio substituted by methoxycarbonyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••halogenated methyl,

•heterocyclyl;

R_2 is methylamino or dimethylamino;

L is selected from Formula XX - XXII;

Y is $-(CH_2)_m$, m is 0 or 1;

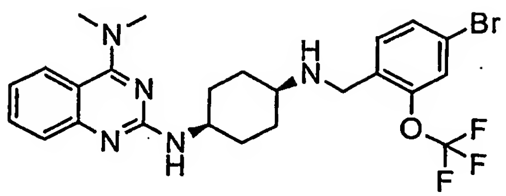
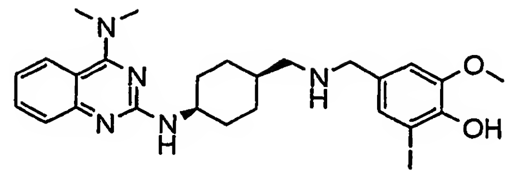
wherein carbocyclic aryl is phenyl, **naphthyl**, or biphenyl;

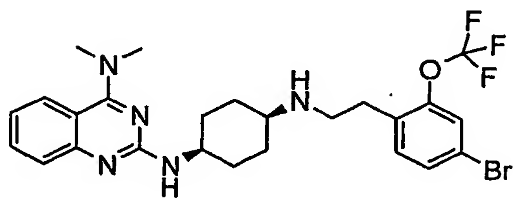
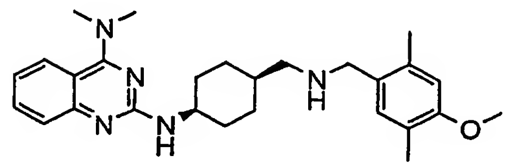
carbocyclyl is acenaphthyl;

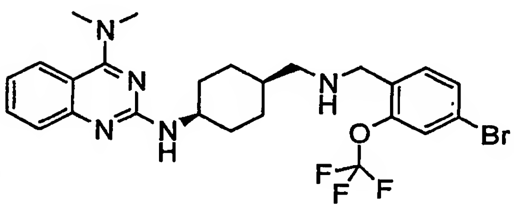
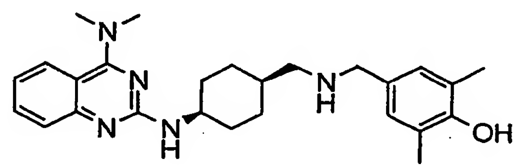
heterocyclyl is 1*H*-indolyl, 1*H*-pyrrolyl, 2,3-dihydro-benzo[1,4]dioxinyl, 9*H*-carbazolyl, benzo[1,3]dioxolyl, furyl, pyrazolyl, thienyl, 4-oxo-benzopyranyl, azetidinyl, imidazo[2,1-b]thiazolyl, pyridyl, imidazolyl, 2,3-dihydro-benzofuryl, or benzo[b]thienyl;;

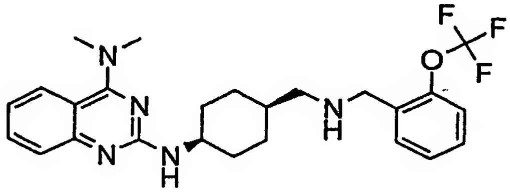
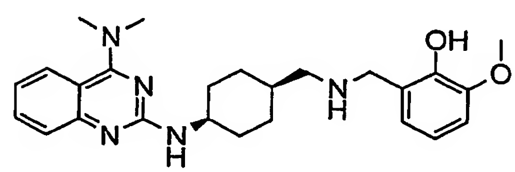
halogen is fluoro, chloro, bromo, or iodo.

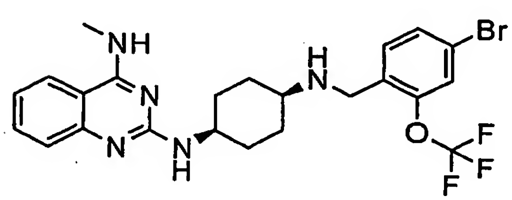
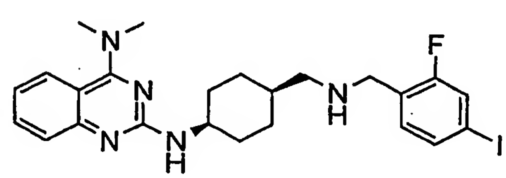
The following compounds are specially preffered;

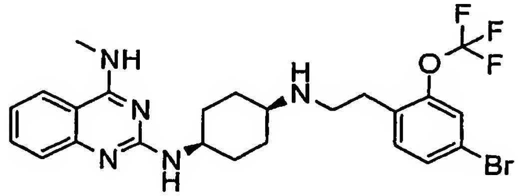
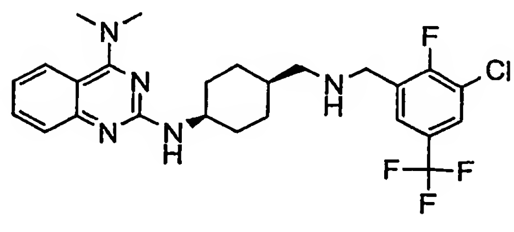
 ,  ,

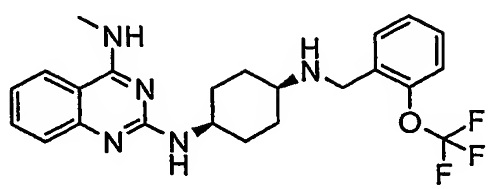
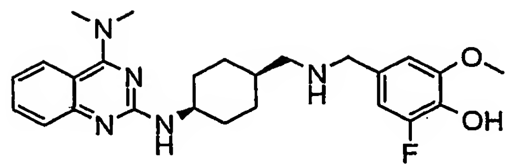
 ,  ,

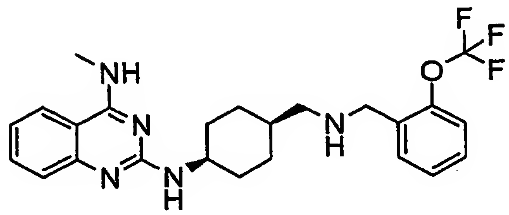
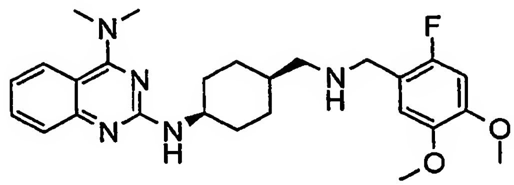
 ,  ,

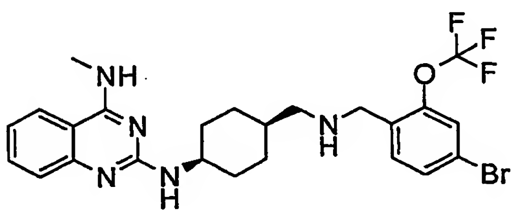
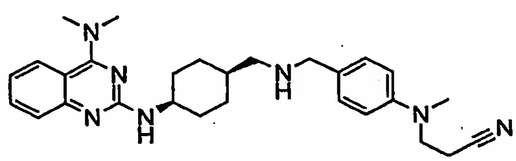
 ,  ,

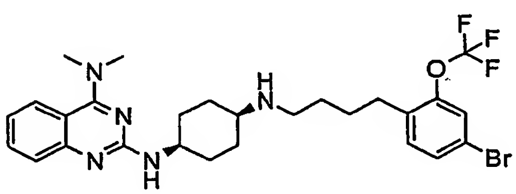
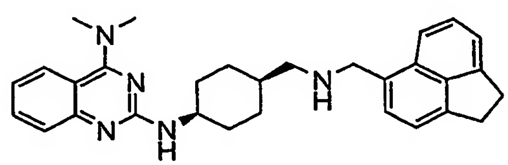
 ,  ,

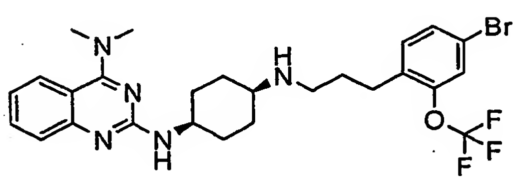
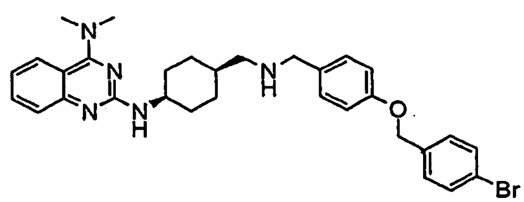
 ,  ,

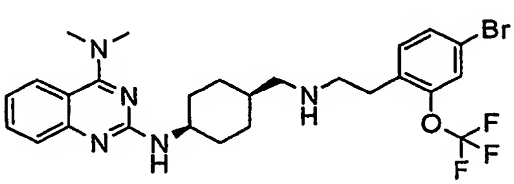
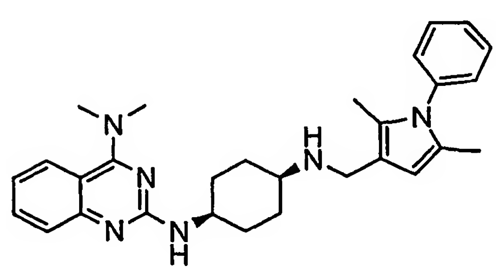
 ,  ,

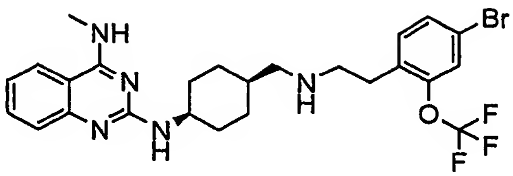
 ,  ,

 ,  ,

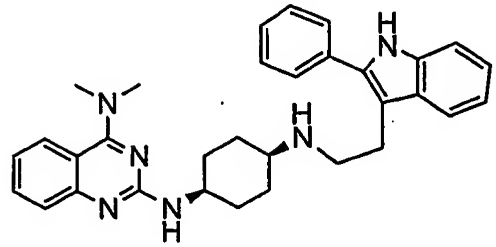
 ,  ,

 ,  ,

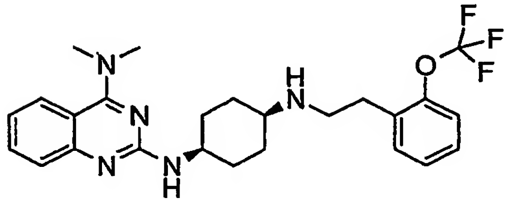
 ,  ,



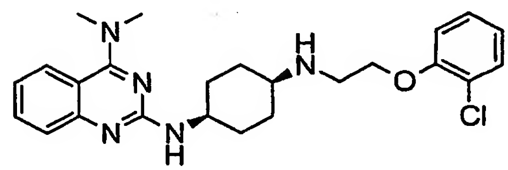
,



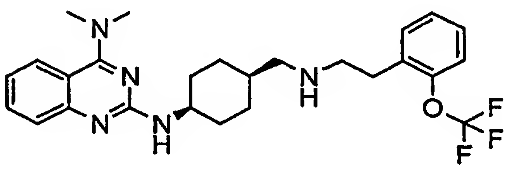
,



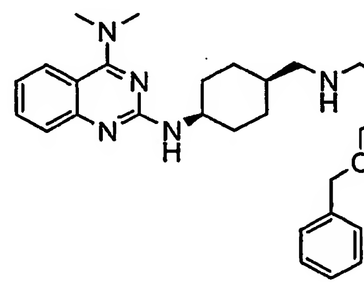
,



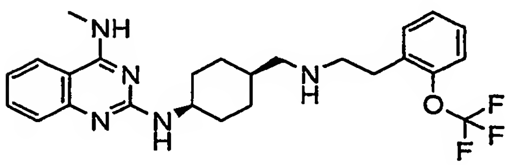
,



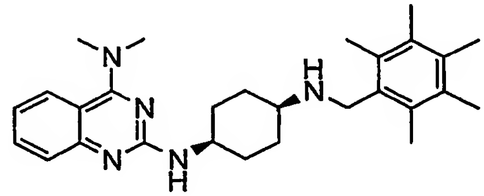
,



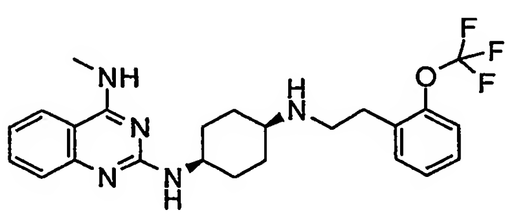
,



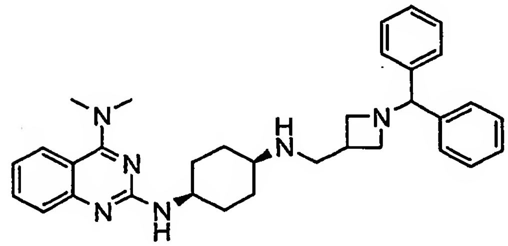
,



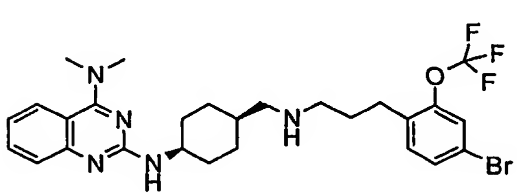
,



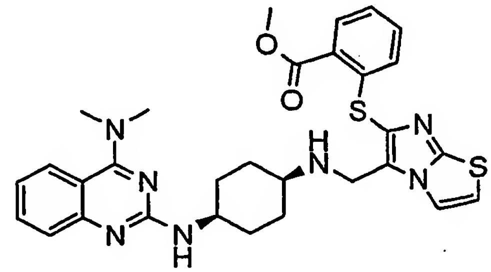
,



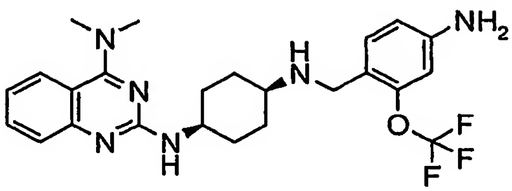
,

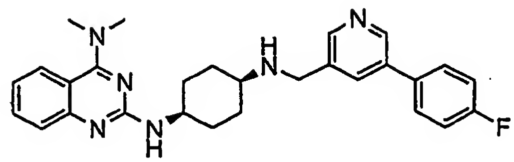


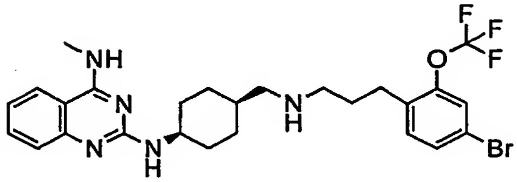
,

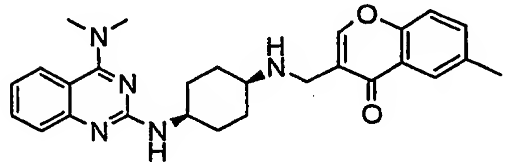


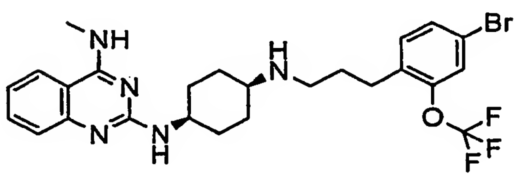
,

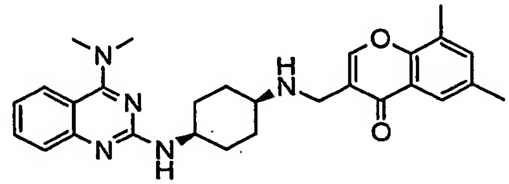
 ,

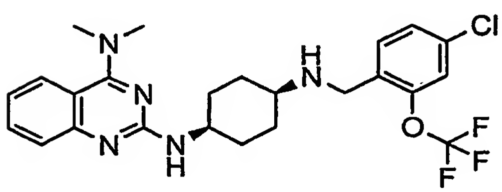
 ,

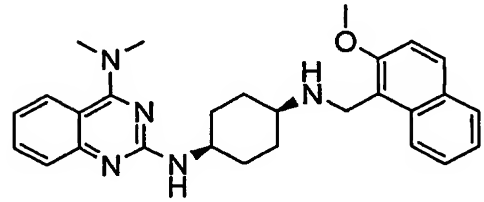
 ,

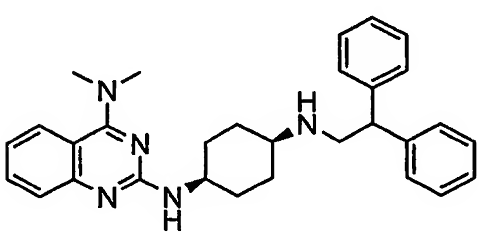
 ,

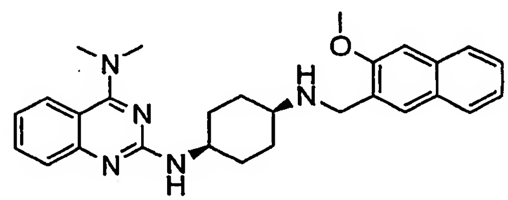
 ,

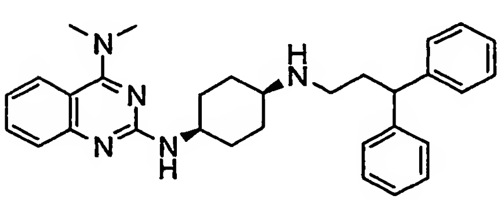
 ,

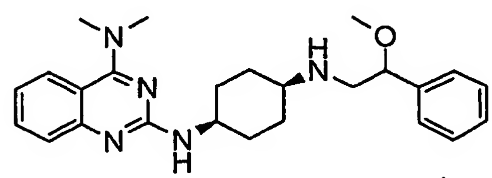
 ,

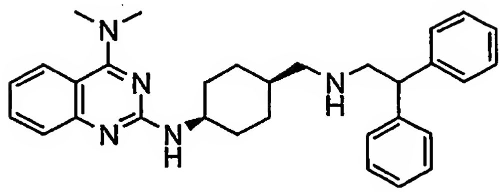
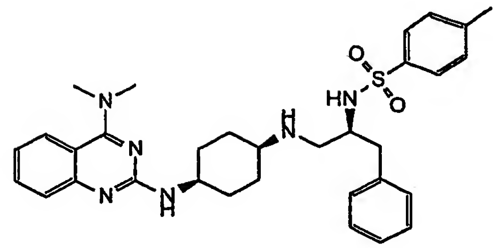
 ,

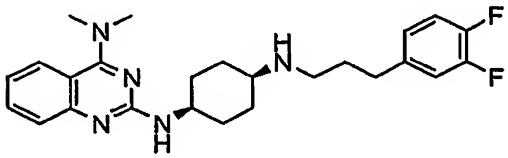
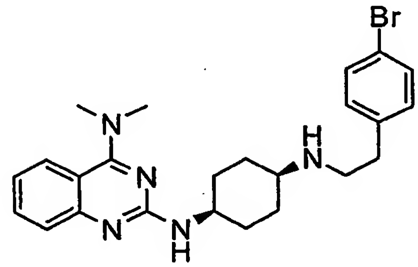
 ,

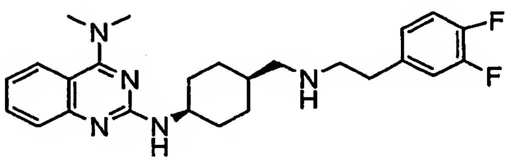
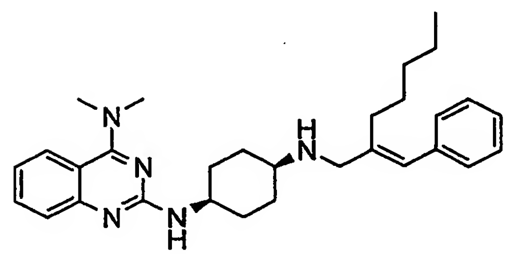
 ,

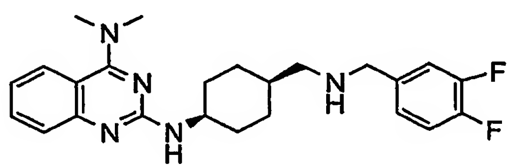
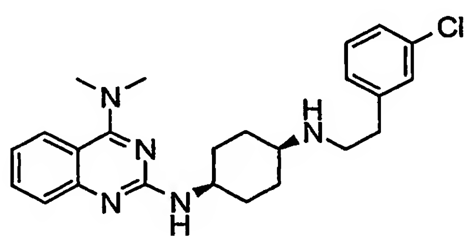
 ,

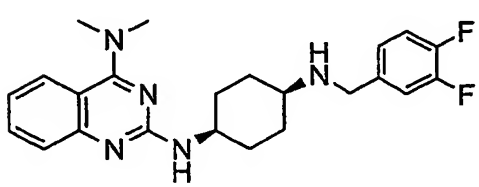
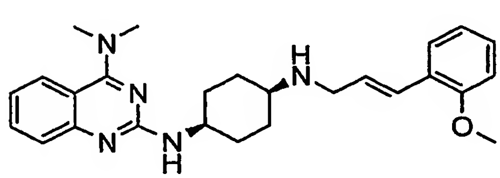
 ,

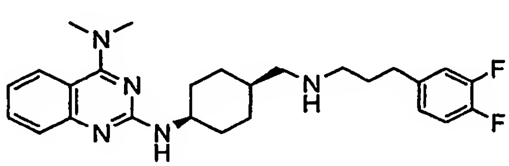
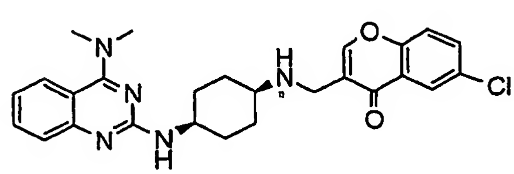

,

,

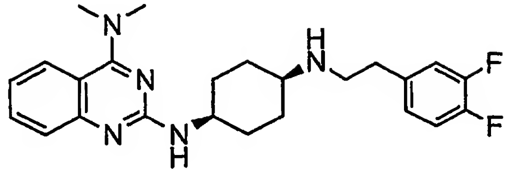
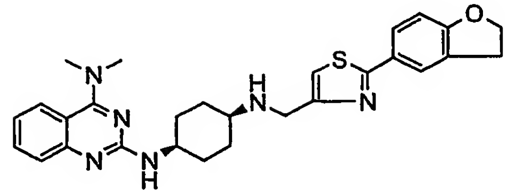

,

,

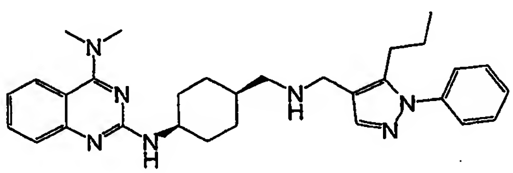
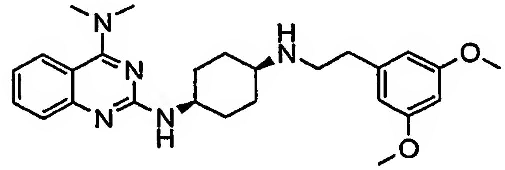

,

,

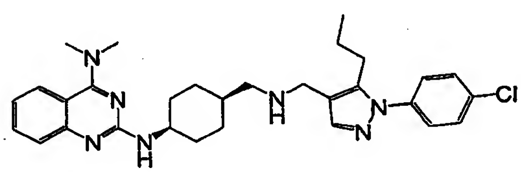
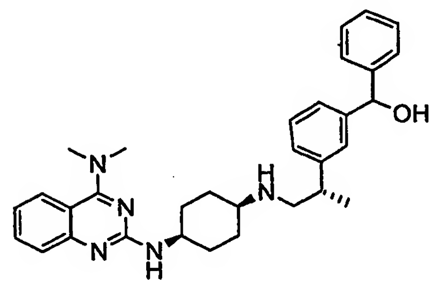

,

,

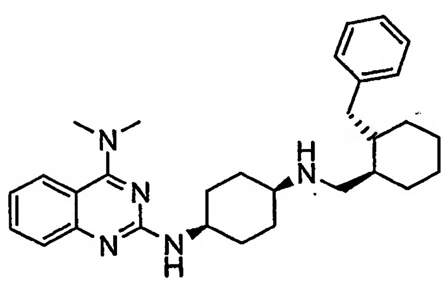
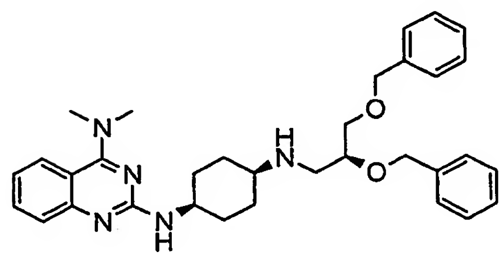

,

,

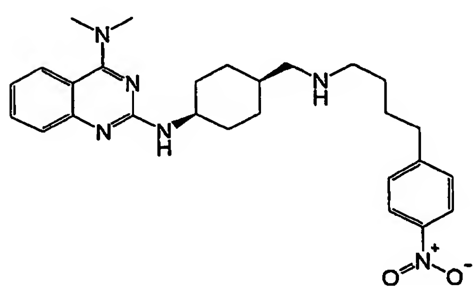
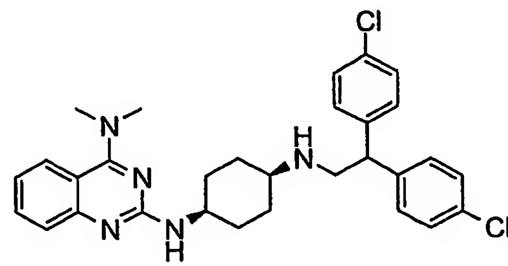

,

,

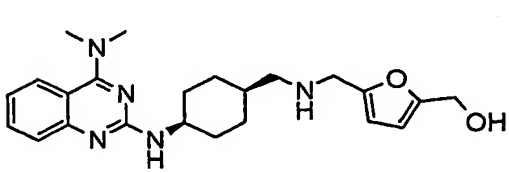
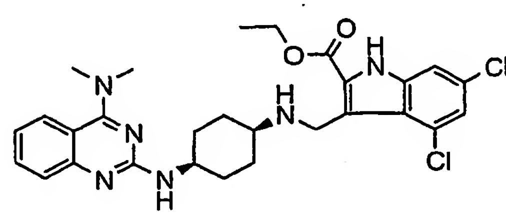
,
,

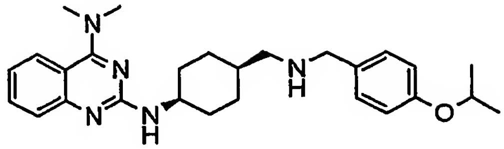
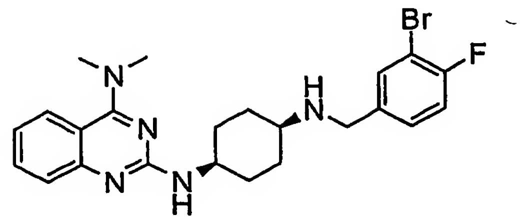
,
,

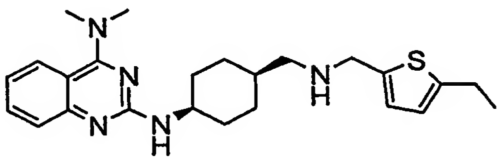
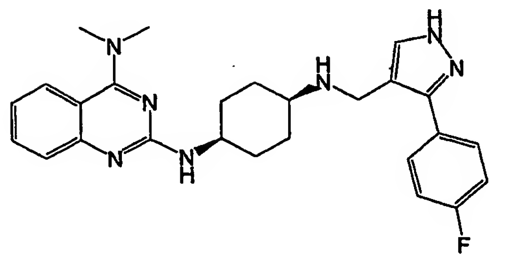
,
,

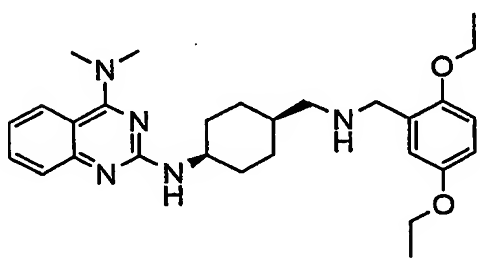
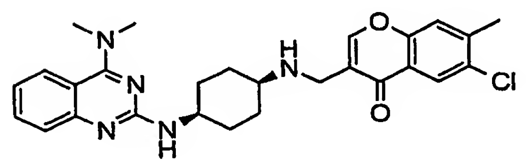
,
,

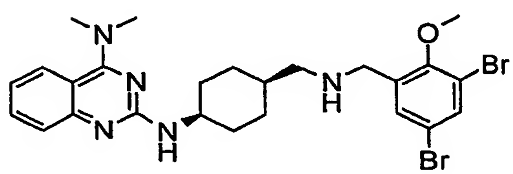
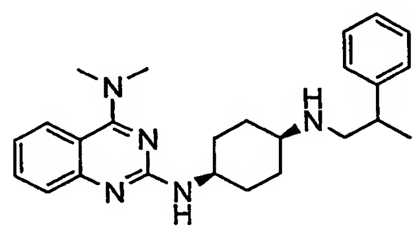
,
,

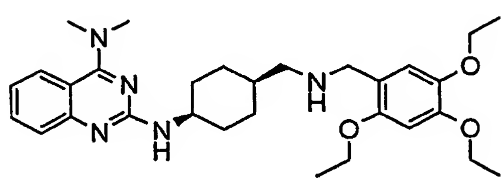
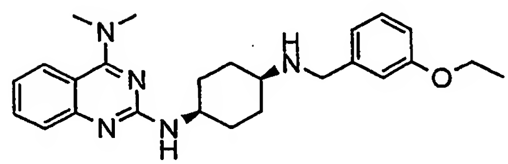
,
,

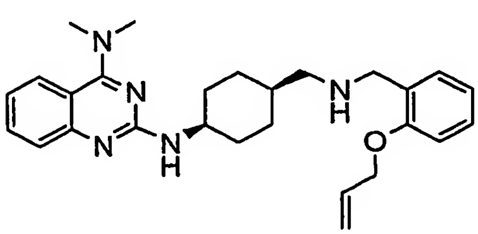
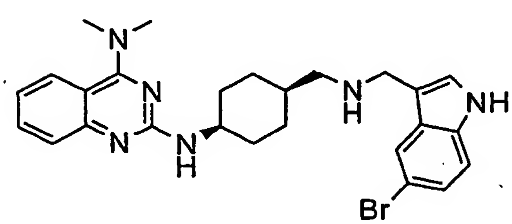

,

,

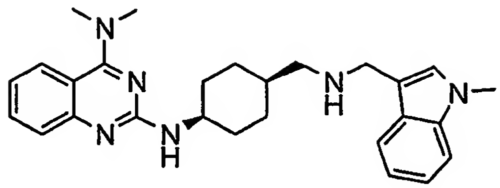
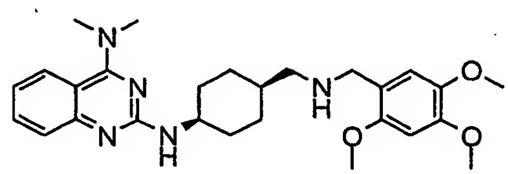
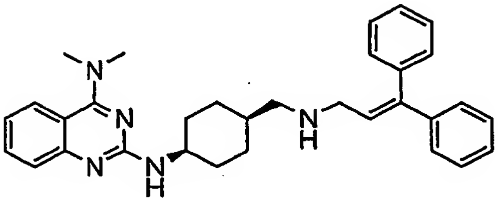
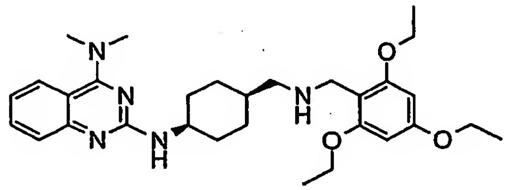
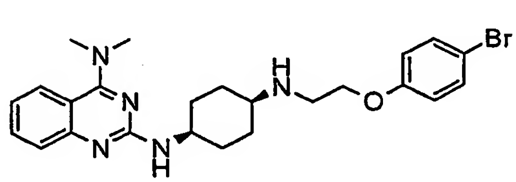
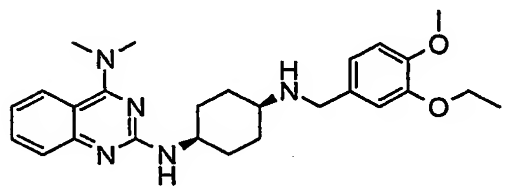
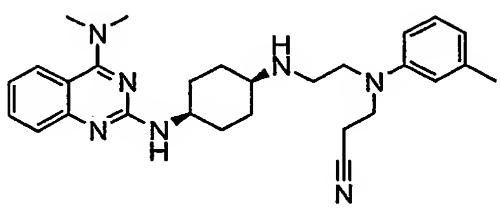
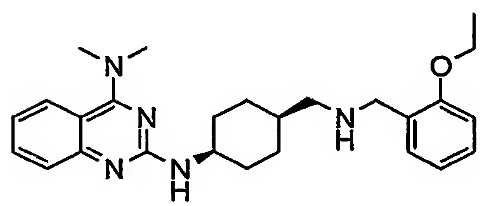
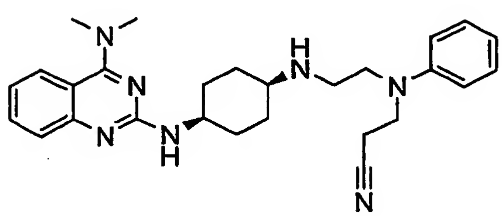
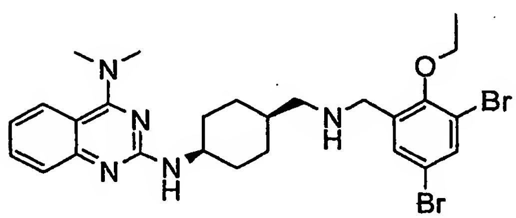
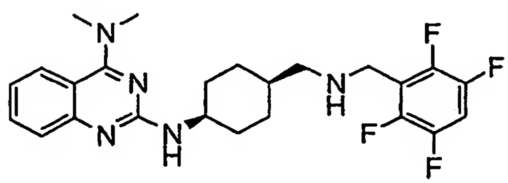
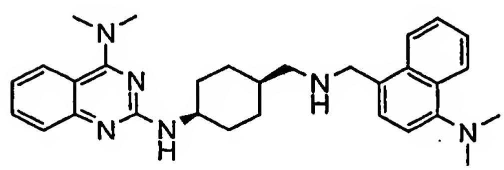

,

,

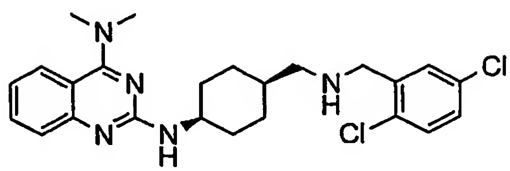
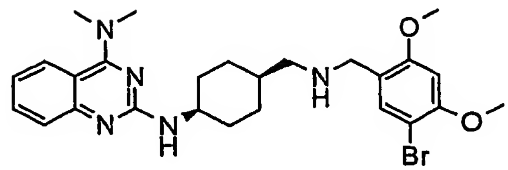

,

,

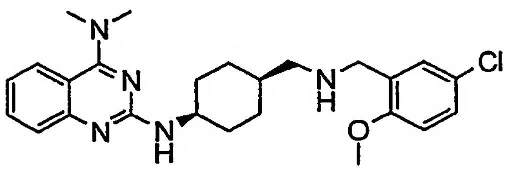
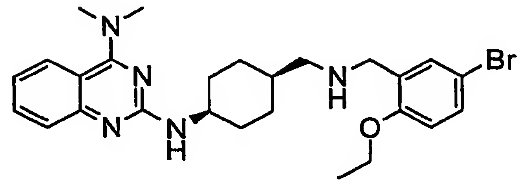

,

,

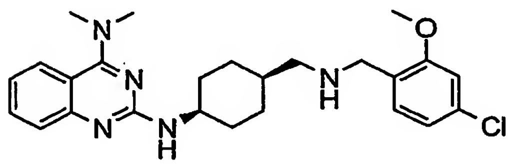
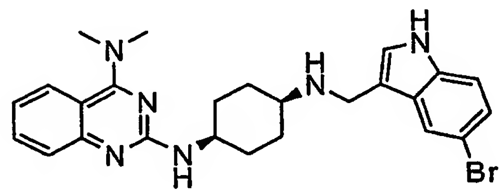

,

,

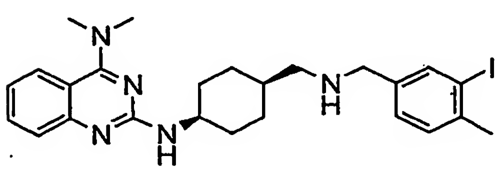
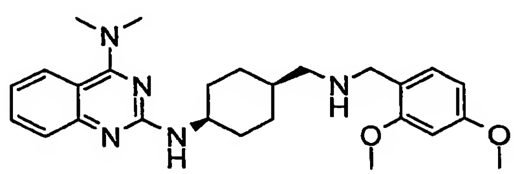

,

,

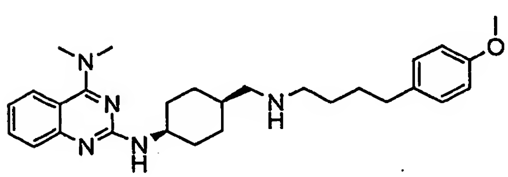
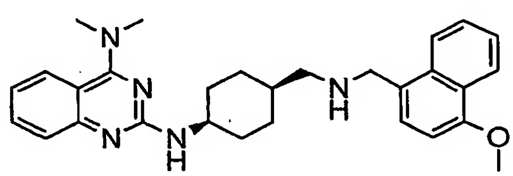
,
,
,
,
,
,
,
,
,
,
,
,

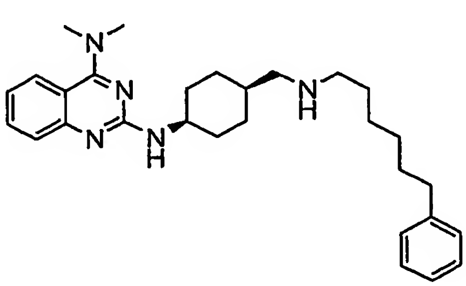
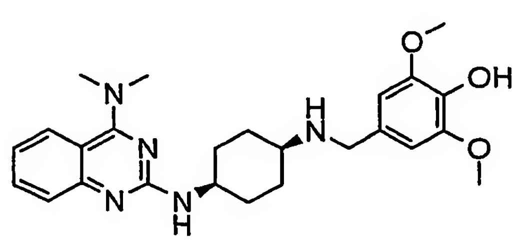
 ,  ,

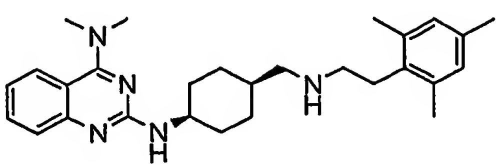
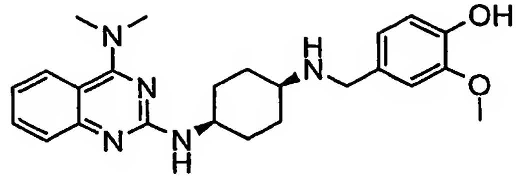
 ,  ,

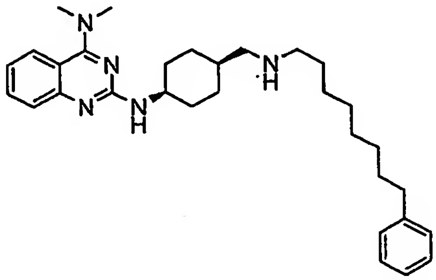
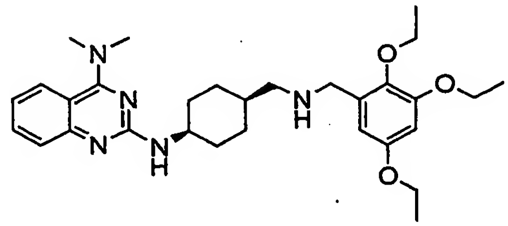
 ,  ,

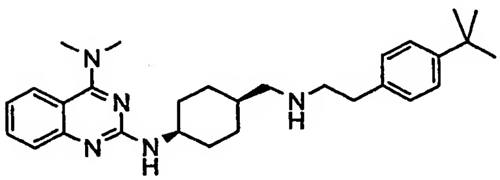
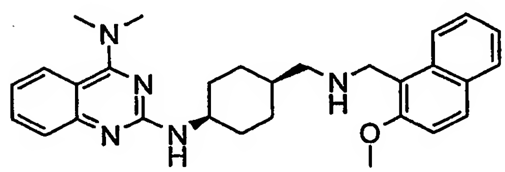
 ,  ,

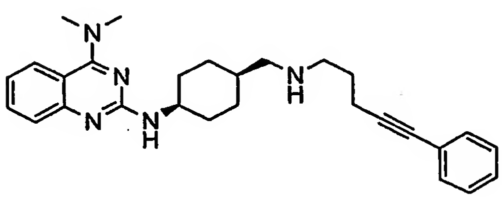
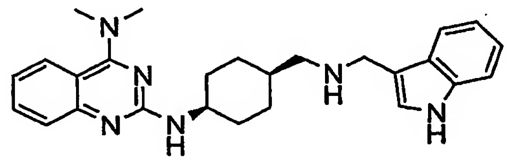
 ,  ,

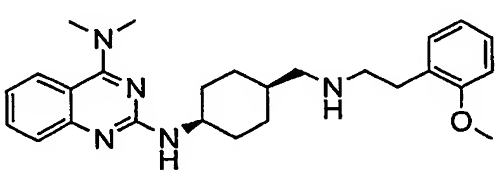
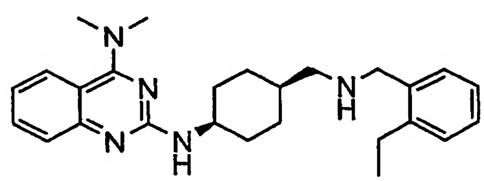
 ,  ,

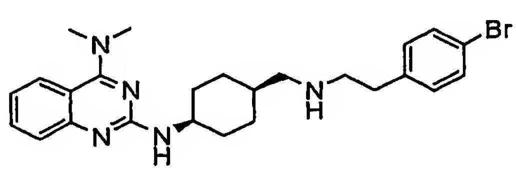
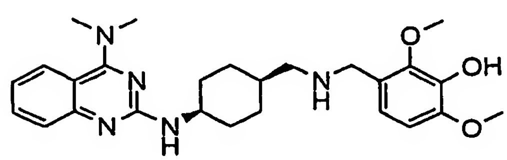
 ,  ,

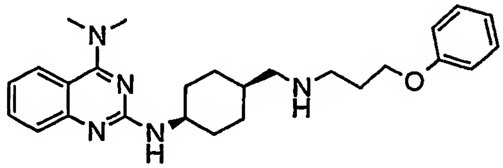
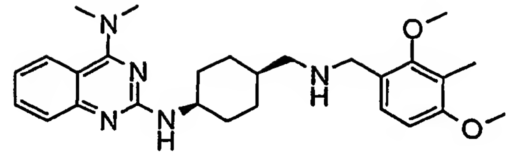
 ,  ,

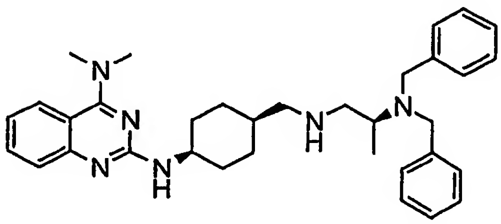
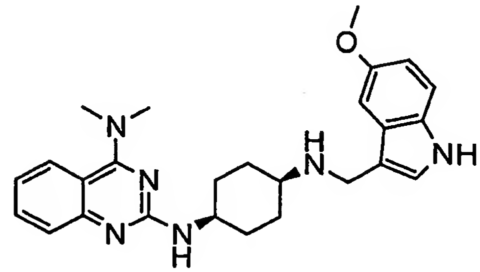
 ,  ,

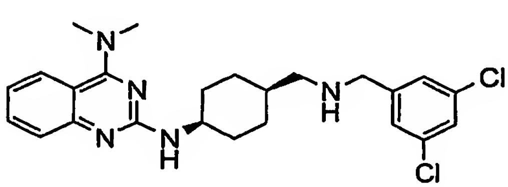
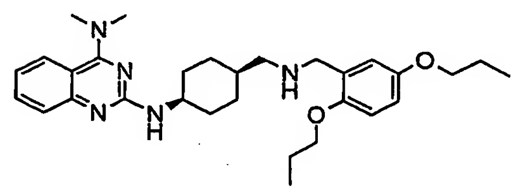
 ,  ,

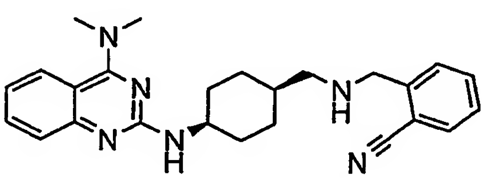
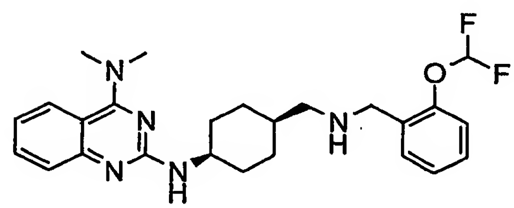
 ,  ,

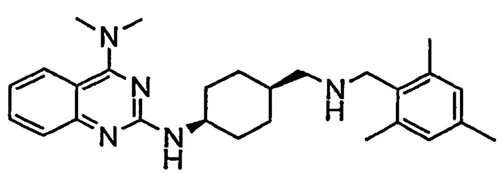
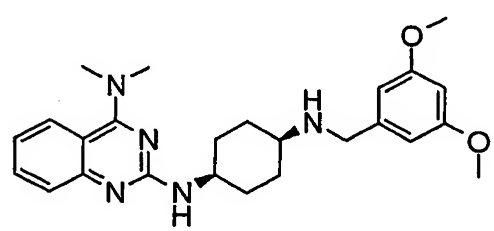
 ,  ,

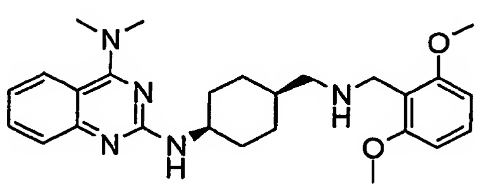
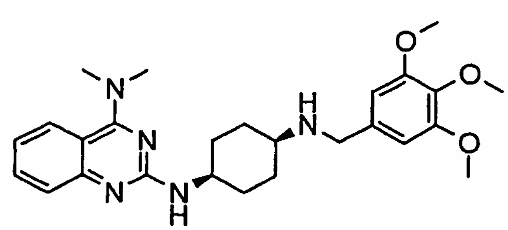

,

,

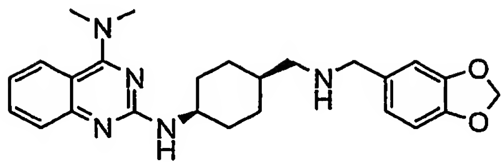
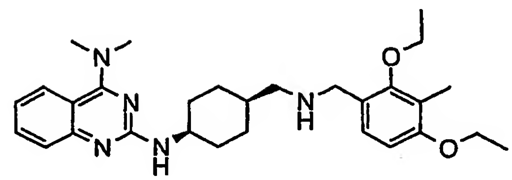

,

,

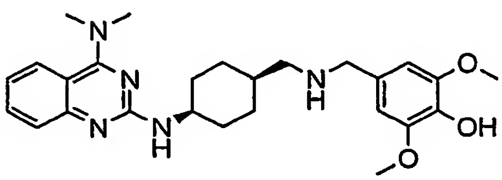
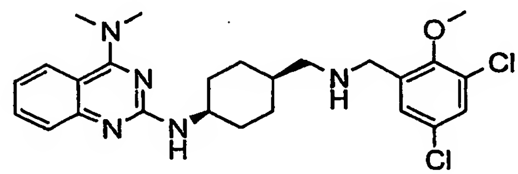

,

,

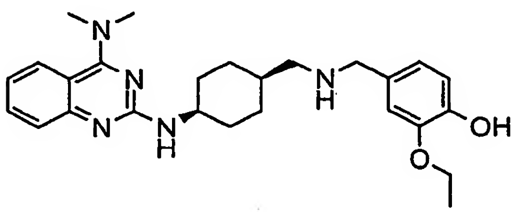
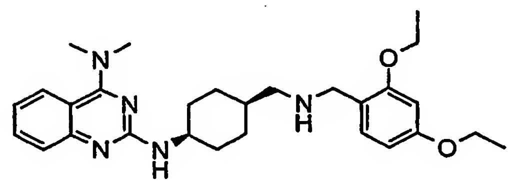

,

,

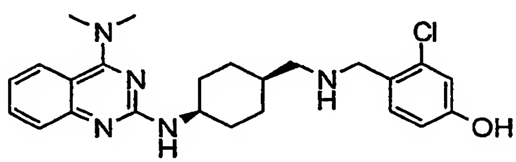
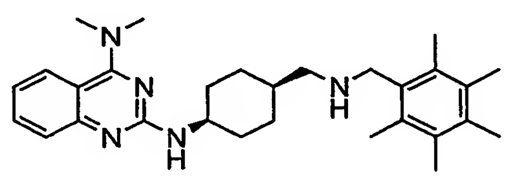

,

,

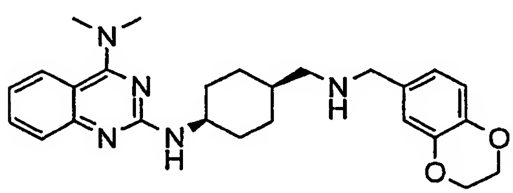
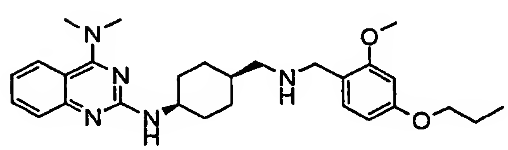

,

,

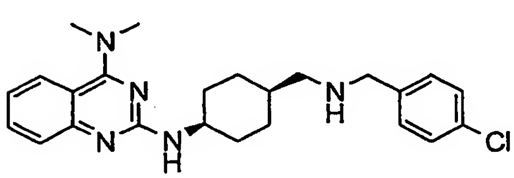
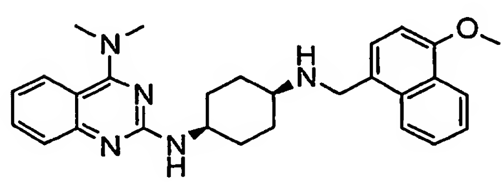
 ,  ,

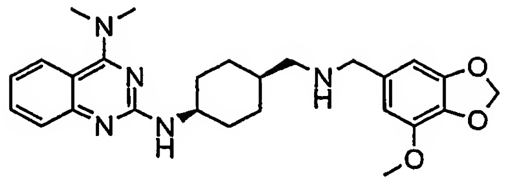
 ,  ,

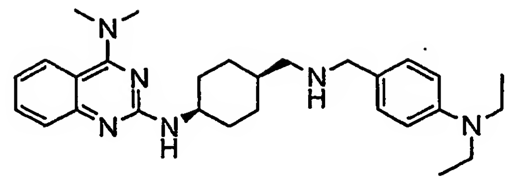
 ,  ,

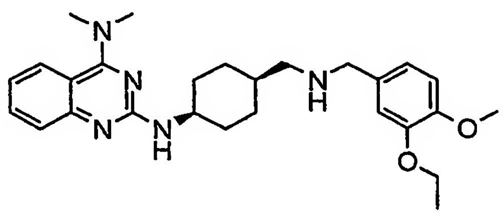
 ,  ,

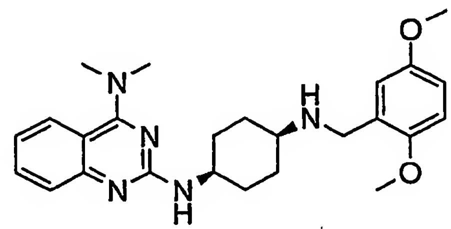
 ,  ,

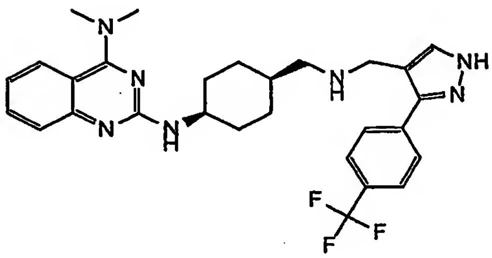
 ,  ,

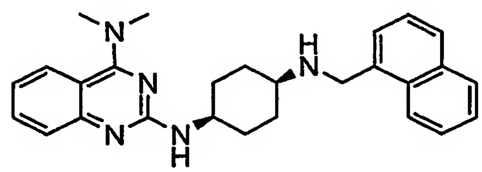

,

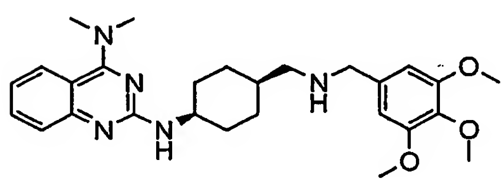

,

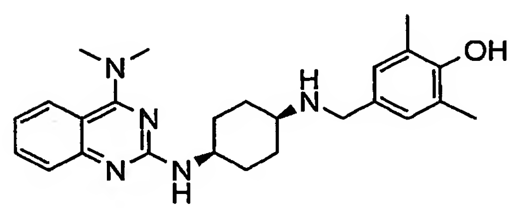

,

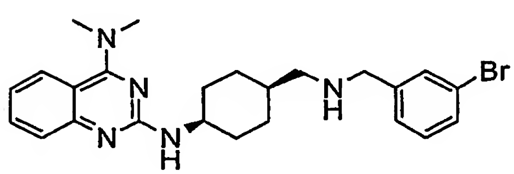

,

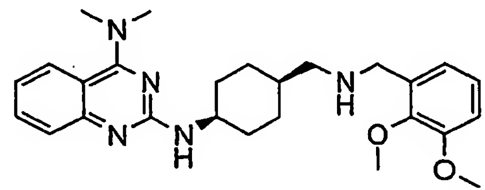

,

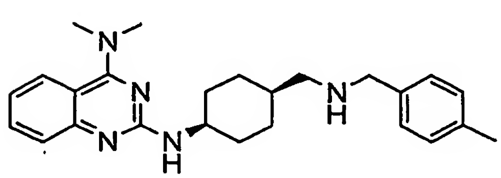

,

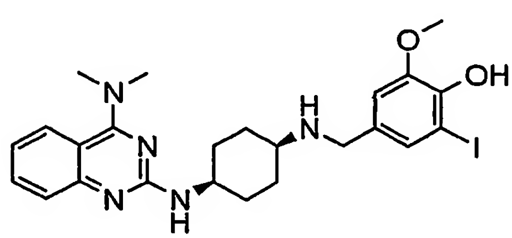

,

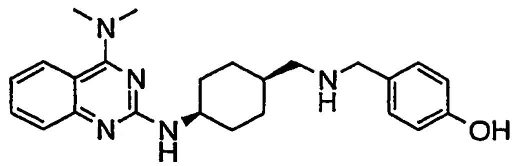

,

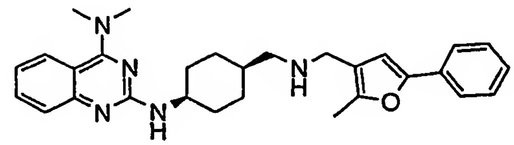

,

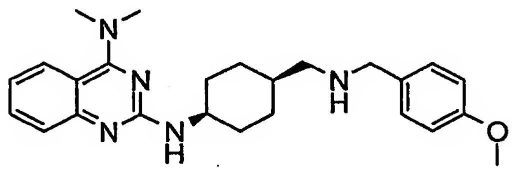

,

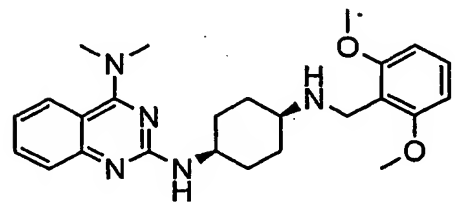

,

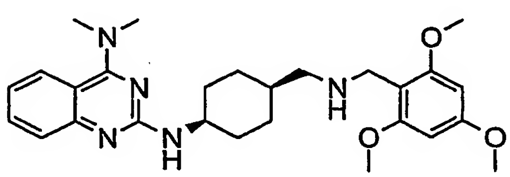

,

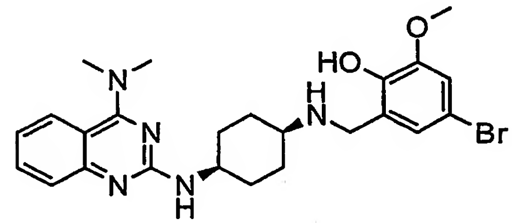
 ,

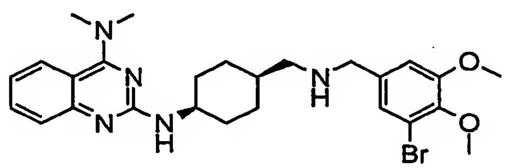
 ,

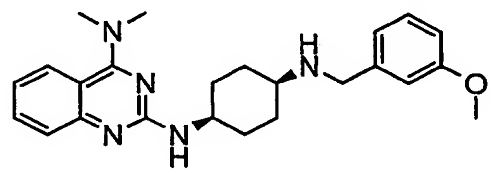
 ,

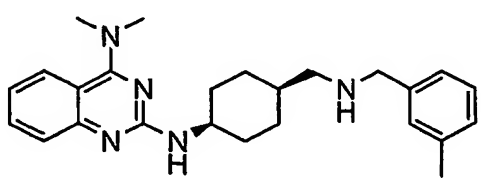
 ,

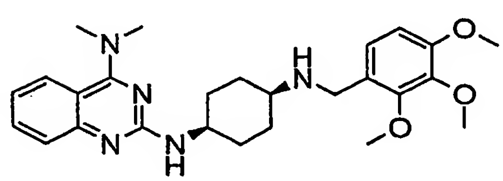
 ,

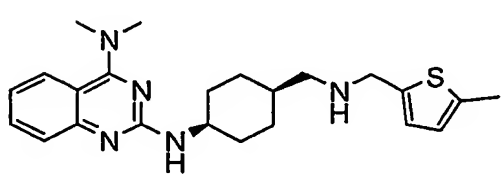
 ,

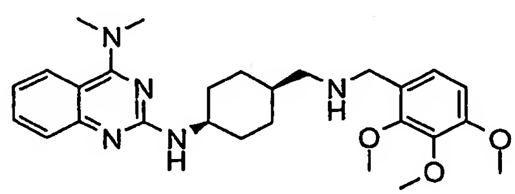
 ,

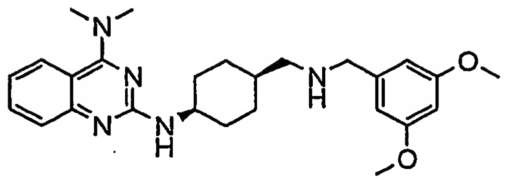
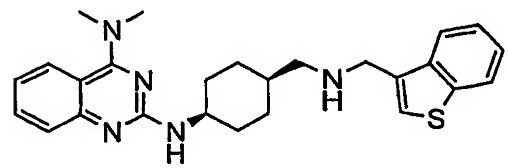
 ,

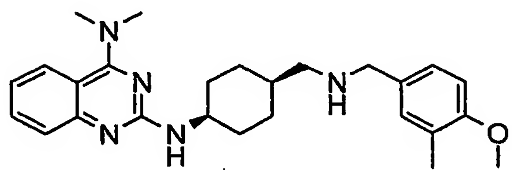
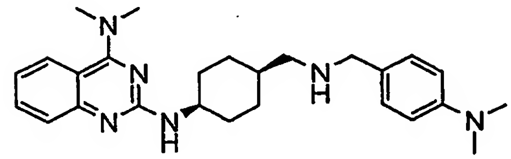
 ,

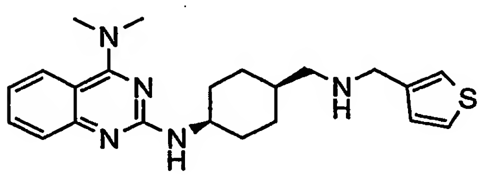
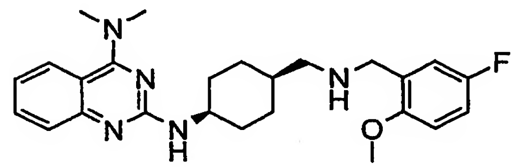
 ,

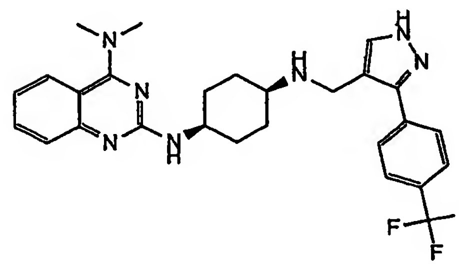
 ,

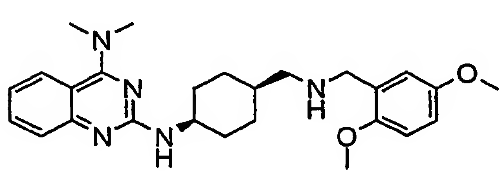
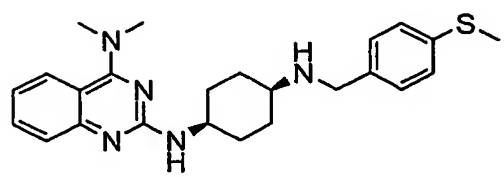
 ,

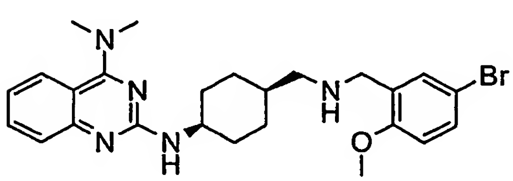
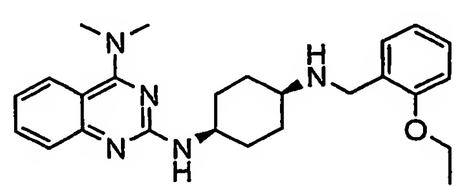

,

,

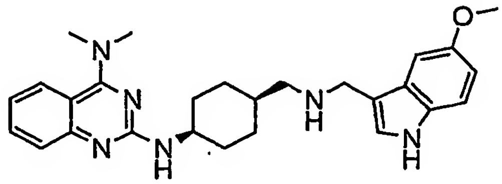
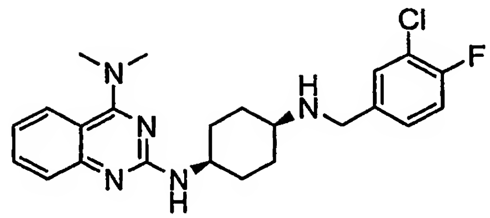

,

,

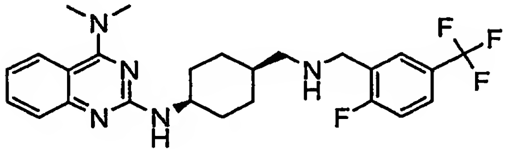
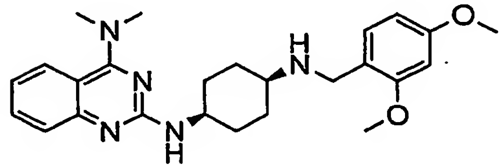

,

,

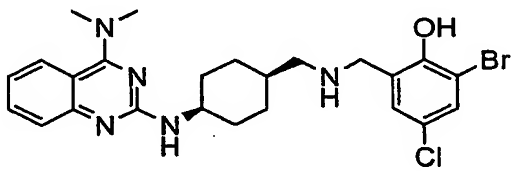
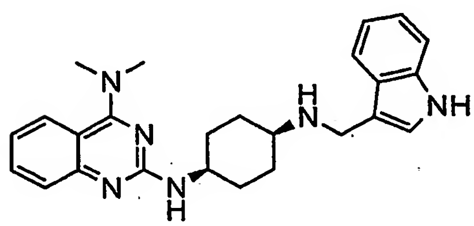

,

,

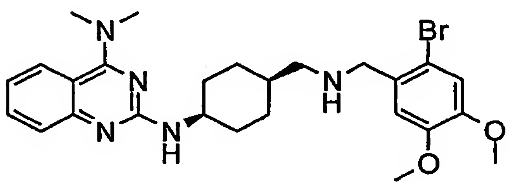

,

,


,

,

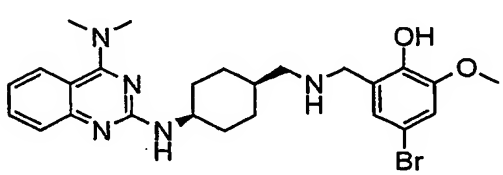
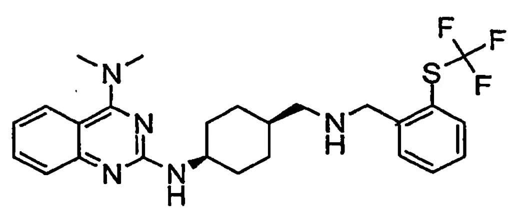

,

,

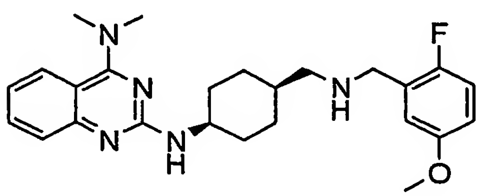
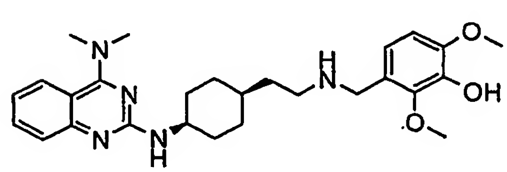

,

,

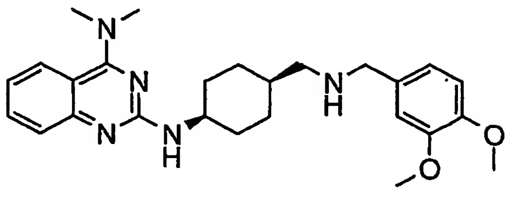
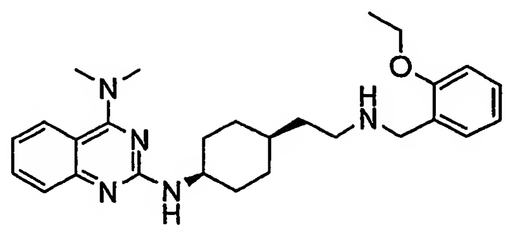

,

,

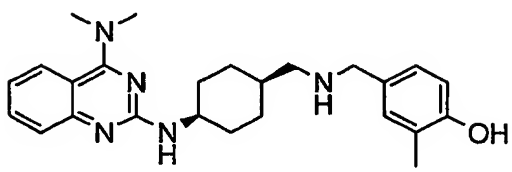
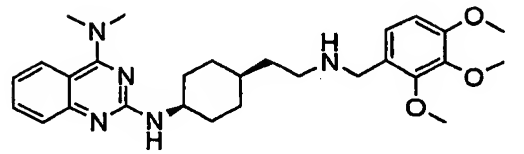

,

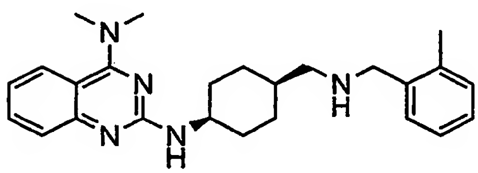
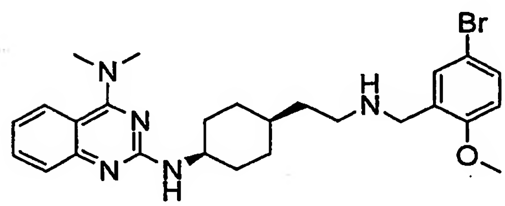
,

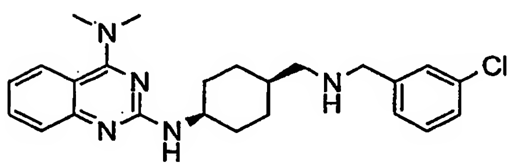
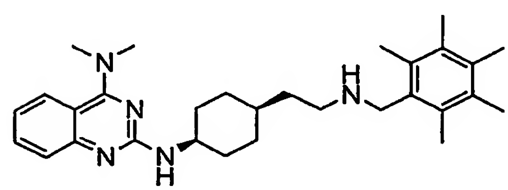

,

,

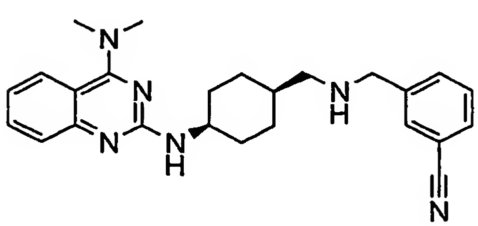
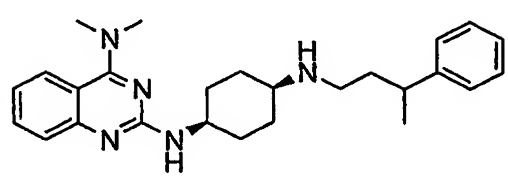

,

,


,

,


,

,


,

,


,

,


, and


; or, in case of, a salt thereof.

Preferred compounds of this invention are those compounds of Formula I wherein,

Q is Formula II;

R_1 represents

(i) C_1-C_{16} alkyl,

C_1-C_{16} alkyl substituted by substituent(s) independently selected from

•halogen,

•carbocyclyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••nitro,

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl,

(ii) C_2-C_3 alkenyl,

C_2-C_3 alkenyl substituted by carbocyclic aryl,

(iii) carbocyclic aryl,

carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•cyano,

•nitro,

•C_1-C_5 alkyl,

•C_1-C_5 alkyl substituted by substituent(s) independently selected from

••halogen,

••oxo,

•C_2-C_3 alkenyl,

•C_1-C_4 alkoxy,

•C_1-C_4 alkoxy substituted by substituent(s) independently selected from

••halogen,

••heterocyclyl,

••halogenated heterocyclyl,

•carbocyclic aryloxy,

•carbocyclic aryloxy substituted by substituent(s) independently selected from

••halogen,

••nitro,

•heterocyclyloxy,

•heterocyclyloxy substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl,

•C_1-C_3 alkoxycarbonyl,

•mono- or di-C_1-C_4 alkylamino,

•C_1-C_3 alkylcarbonylamino,

•carbocyclic aryl diazo,

•carbocyclic aryl diazo substituted by mono- or di- C_1-C_3 alkylamino,

•C_1-C_3 alkylsulfonyl,

•carbocyclic aryl,

(iv) heterocyclyl,

or heterocyclyl substituted by substituent(s) independently selected from

•halogen,

•C_1-C_3 alkyl,

• C_1-C_3 alkyl substituted by substituent(s) independently selected from

••halogen,

••oxo,

••carbocyclic arylcarbonylamino,

••halogenated carbocyclic arylcarbonylamino,

••heterocyclyl,

••heterocyclyl substituted by substituent(s) independently selected from

•••halogen,

•••C_1-C_3 alkyl,

•••halogenated C_1-C_3 alkyl,

•C_1-C_3 alkoxy,

•C_1-C_3 alkylcarbonylamino,

•carbocyclic arylsulfonyl,

•C_1-C_3 alkoxycarbonyl,

•carbocyclic aryl,

•halogenated carbocyclic aryl,

•heterocyclyl,

•heterocyclyl substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••halogenated C_1-C_3 alkyl;

R_2 is -$NHNH_2$, -NHNHBoc, -$N(R_{2a})(R_{2b})$; morpholino, 4-acetyl-piperazyl, or 4-phenyl-piperazyl;

wherein R_{2a} is H or C_1-C_3 alkyl;

R_{2b} is C_1-C_4 alkyl, C_1-C_4 alkyl substituted by substituent(s) independently selected from

•hydroxy,

•C_1-C_3 alkoxy,

•amino,

•-NHBoc,

•C_3-C_6 cycloalkyl,

•carbocyclic aryl,

•carbocyclic aryl substituted by substituent(s) independently selected from

••halogen,

••C_1-C_3 alkyl,

••C_1-C_3 alkoxy,

••-SO_2NH_2,

•heterocyclyl,

C_3-C_6 cycloalkyl, carbocyclic aryl, carbocyclic aryl substituted by substituent(s) independently selected from

•halogen,

•C_1-C_3 alkyl,

•C_1-C_3 alkoxy,

or a group of Formula IV;

wherein Boc is carbamic acid *tert*-butyl ester and R_3 is C_1-C_3 alkyl or C_1-C_3 alkyl substituted by substituent(s) independently selected from

•carbocyclic aryl,

•halogenated carbocyclic aryl,

•carbocyclic aryl substituted by C_1-C_3 alkoxy;

L is selected from Formula V - XIX;

wherein R_4 is H or C_1-C_3 alkyl;

R_5 is H, C_1-C_3 alkyl, or C_1-C_3 alkyl substituted by a substituted carbocyclic aryl;

Y is $-S(O)_2-$;

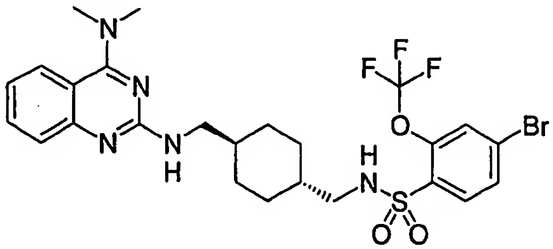
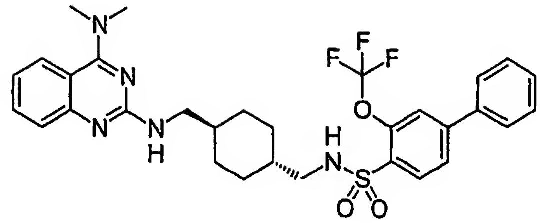
wherein carbocyclic aryl is phenyl, naphthyl, or biphenyl;

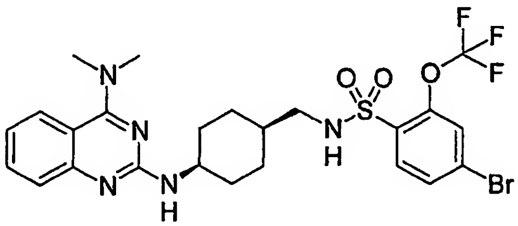
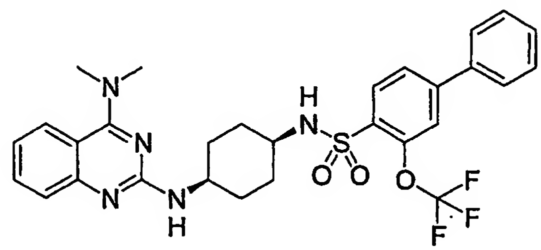
carbocyclyl is 7,7-dimethyl-2-oxo-bicyclo[2.2.1]heptyl;

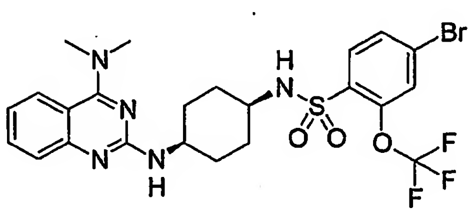
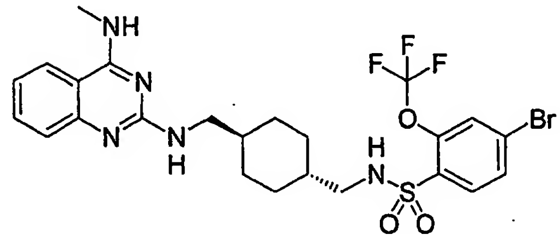
heterocyclyl is 1,2,3,4-tetrahydro-isoquinolyl, 1,2,3-thiadiazolyl, 1*H*-pyrrolyl, benzo[2,1,3]oxadiazolyl, benzo[b]thienyl, furyl, imidazolyl, isoxazolyl, pyrazolyl, pyridyl, quinolyl, thiazolyl, or thienyl;

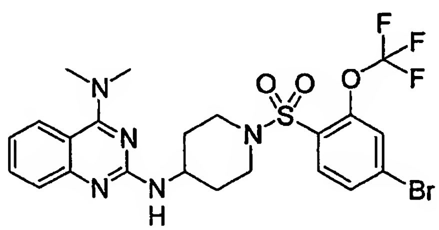
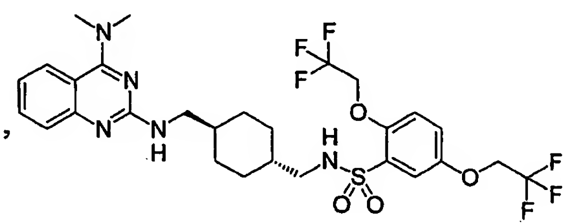
halogen is fluoro, chloro, bromo, or iodo.

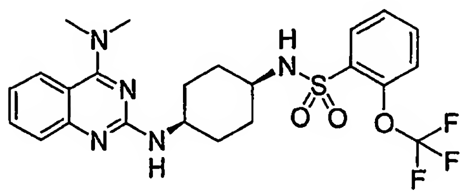
The following compounds are specially preffered;

 ,  ,

 ,  ,

 ,  ,

 ,  ,

and 

; or, in case of, a salt thereof.

Preferred compounds of this invention are those compounds of Formula I wherein,

Q is Fomura II;

R_1 is selected from H, $-CO_2{}^tBu$, or $-CO_2Bn$ (Bn is a benzyl group);

R_2 is methylamino or dimethylamino;

L is selected from Formula XX - XXII;

Y is a single bond;

or a salt thereof.

One embodiment of the invention includes any compound of the invention which selectively binds an MCH receptor, such selective binding is preferably demonstrated by a Ki for one or more other GPCR(s), preferably NPY, being at least 10-fold greater than the Ki for any particular MCH receptor, preferable MCHR1.

As used herein, the term "alkyl" is intended to denote hydrocarbon compounds including straight chain and branched chain, including for example but not limited to methyl, ethyl, n-propyl, isopropyl, n-butyl, sec-butyl, tert-butyl, n-pentyl, isopentyl, tert-pentyl, n-hexyl, and the like.

The term "alkoxy" is intended to denote substituents of the formula -O-alkyl.

At various places in the present specification substituents of compounds of the invention are disclosed in groups. It is specifically intended that the invention include each and every individual subcombination of the members of such groups.

G-protein coupled receptors (GPCRs) represent a major class of cell surface receptors with which many neurotransmitters interact to mediate their effects. GPCRs are predicted to have seven membrane-spanning domains and are coupled to their effectors via G-proteins linking receptor activation with intracellular biochemical sequelae such as stimulation of adenylyl cyclase. Melanin Concentrating Hormone (MCH), a cyclic peptide, has been identified as the endogenous ligand of the orphan G-protein coupled receptor SLC-1. See, for example, Shimomura et al., Biochem. Biophys. Res. Commun. 261, 622-26 (1999). Studies have indicated that MCH acts as a neurotransmitter/modulator/regulator to alter a number of behavioral responses.

Mammalian MCH (19 amino acids) is highly conserved between rat, mouse, and human, exhibiting 100% amino acid identity, but its physiological roles are less clear. MCH

has been reported to participate in a variety of processes including feeding, water balance, energy metabolism, general arousal/attention state, memory and cognitive functions, and psychiatric disorders. For reviews, see 1. Baker, Int. Rev. Cytol. 126:1-47 (1991); 2. Baker, TEM 5:120-126 (1994); 3. Nahon, Critical Rev. in Neurobiol 221:221-262, (1994); 4. Knigge et al., Peptides 18(7):1095-1097, (1996). The role of MCH in feeding or body weight regulation is supported by Qu et al., Nature 380:243-247, (1996), demonstrating that MCH is over expressed in the hypothalamus of ob/ob mice compared with ob/+mice, and that fasting further increased MCH mRNA in both obese and normal mice during fasting. MCH also stimulated feeding in normal rats when injected into the lateral ventricles as reported by Rossi et al., Endocrinology 138:351-355, (1997). MCH also has been reported to functionally antagonize the behavioral effects of α-MSH; see: Miller et al., Peptides 14:1-10, (1993); Gonzalez et al, Peptides 17:171-177, (1996); and Sanchez et al., Peptides 18:3933-396, (1997). In addition, stress has been shown to increase POMC mRNA levels while decreasing the MCH precursor preproMCH (ppMCH) mRNA levels; Presse et al., Endocrinology 131:1241-1250, (1992). Thus MCH may serve as an integrative neuropeptide involved in the reaction to stress, as well as in the regulation of feeding and sexual activity; Baker, Int. Rev. Cytol. 126:1-47, (1991); Knigge et al., Peptides 17:1063-1073, (1996).

The localization and biological activities of MCH peptide suggest that the modulation of MCH receptor activity may be useful in a number of therapeutic applications. MCH is expressed in the lateral hypothalamus, a brain area implicated in the regulation of thirst and hunger: Grillon et al., Neuropeptides 31:131-136, (1997); recently orexins A and B, which are potent orexigenic agents, have been shown to have very similar localization to MCH in the lateral hypothalamus; Sakurai et al., Cell 92:573-585 (1998). MCH mRNA levels in this brain region are increased in rats after 24 hours of food-deprivation; Herve and Fellmann, Neurpeptides 31:237-242 (1997); after insulin injection, a significant increase in the abundance and staining intensity of MCH immunoreactive perikarya and fibres was observed concurrent with a significant increase in the level of MCH mRNA; Bahjaoui-Bouhaddi et al., Neuropeptides 24:251-258, (1994). Consistent with the ability of MCH to stimulate feeding in rats; Rossi et al., Endocrinology 138:351-355, (1997); is the observation that MCH mRNA levels are upregulated in the hypothalami of obese ob/ob mice; Qu et al., Nature 380:243-247, (1996); and decreased in the hypothalami of rats treated with leptin,

whose food intake and body weight gains are also decreased; Sahu, Endocrinology 139:795-798, (1998). MCH appears to act as a functional antagonist of the melanocortin system in its effects on food intake and on hormone secretion within the HPA (hypothalamopituitary/adrenal axis); Ludwig et al., Am. J. Physiol. Endocrinol. Metab. 274:E627-E633, (1998). Together these data suggest a role for endogenous MCH in the regulation of energy balance and response to stress, and provide a rationale for the development of specific compounds acting at MCH receptors for use in the treatment of obesity and stress-related disorders.

Accordingly, a MCH receptor antagonist is desirable for the prophylaxis or treatment of obesity or obesity related disorders. An obesity related disorder is a disorder that has been directly or indirectly associated to obesity, such as, type II diabetes, syndrome X, impaired glucose tolerance, dyslipidaemia, hypertension, coronary heart disease and other cardiovascular disorders including atherosclerosis, insulin resistance associated with obesity and psoriasis, for treating diabetic complications and other diseases such as polycystic ovarian syndrome (PCOS), certain renal diseases including diabetic nephropathy, glomerulonephritis, glomerular sclerosis, nephrotic syndrome, hypertensive nephrosclerosis, end-stage renal diseases and microalbuminuria as well as certain eating disorders.

In species studied to date, a major portion of the neurons of the MCH cell group occupies a rather constant location in those areas of the lateral hypothalamus and subthalamus where they lie and may be a part of some of the so-called "extrapyramidal" motor circuits. These involve substantial striato- and pallidofugal pathways involving the thalamus and cerebral cortex, hypothalamic areas, and reciprocal connections to subthalamic nucleus, substantia nigra, and mid-brain centers; Bittencourt et al., J. Comp. Neurol. 319:218-245, (1992). In their location, the MCH cell group may offer a bridge or mechanism for expressing hypothalamic visceral activity with appropriate and coordinated motor activity. Clinically it may be of some value to consider the involvement of this MCH system in movement disorders, such as Parkinson's disease and Huntingdon's Chorea in which extrapyramidal circuits are known to be involved.

Human genetic linkage studies have located authentic hMCH loci on chromosome 12 (12q23-24) and the variant hMCH loci on chromosome 5 (5q12-13) (Pedeutour et al., 1994). Locus 12q23-24 coincides with a locus to which autosomal dominant cerebellar ataxia type II (SCA2) has been mapped; Auburger et al., Cytogenet. Cell. Genet. 61:252-256,

(1992); Twells et al., Cytogenet. Cell. Genet. 61:262-265, (1992). This disease comprises neurodegenerative disorders, including an olivopontocerebellar atrophy. Furthermore, the gene for Darier's disease, has been mapped to locus 12q23-24; Craddock et al., Hum. Mol. Genet. 2:1941-1943, (1993). Dariers' disease is characterized by abnormalities I keratinocyte adhesion and mental illnesses in some families. In view of the functional and neuroanatomical patterns of the MCH neural system in the rat and human brains, the MCH gene may represent a good candidate for SCA2 or Darier's disease. Interestingly, diseases with high social impact have been mapped to this locus. Indeed, the gene responsible for chronic or acute forms of spinal muscular atrophies has been assigned to chromosome 5q12-13 using genetic linkage analysis; Melki et al., Nature (London) 344:767-768, (1990); Westbrook et al., Cytogenet. Cell. Genet. 61:225-231, (1992). Furthermore, independent lines of evidence support the assignment of a major schizophrenia locus to chromosome 5q11.2-13.3; Sherrington et al., Nature (London) 336:164-167, (1988); Bassett et al., Lancet 1:799-801, (1988); Gilliam et al., Genomics 5:940-944, (1989). The above studies suggest that MCH may play a role in neurodegenerative diseases and disorders of emotion.

Additional therapeutic applications for MCH-related compounds are suggested by the observed effects of MCH in other biological systems. For example, MCH may regulate reproductive functions in male and female rats. MCH transcripts and MCH peptide were found within germ cells in testes of adult rats, suggesting that MCH may participate in stem cell renewal and/or differentiation of early spermatocytes; Hervieu et al., Biology of Reduction 54:1161-1172, (1996). MCH injected directly into the medial preoptic area (MPOA) or ventromedial nucleus (VMN) stimulated sexual activity in female rats; Gonzalez et al., Peptides 17:171-177, (1996). In ovariectomized rats primed with estradiol, MCH stimulated luteinizing hormone (LH) release while anti-MCH antiserum inhibited LH release; Gonzalez et al., Neuroendocrinology 66:254-262, (1997). The zona incerta, which contains a large population of MCH cell bodies, has previously been identified as a regulatory site for the pre-ovulatory LH surge; MacKenzie et al., Neuroendocrinology 39:289-295, (1984). MCH has been reported to influence release of pituitary hormones including ACTH and oxytocin. MCH analogues may also be useful in treating epilepsy. In the PTZ seizure model, injection of MCH prior to seizure induction prevented seizure activity in both rats and guinea pigs, suggesting that MCH-containing neurons may participate in the neural circuitry underlying PTZ-induced seizure; Knigge and Wagner,

Peptides 18:1095-1097, (1997). MCH has also been observed to affect behavioral correlates of cognitive functions. MCH treatment hastened extinction of the passive avoidance response in rats; McBride et al., Peptides 15:757-759, (1994); raising the possibility that MCH receptor antagonists may be beneficial for memory storage and/or retention. A possible role for MCH in the modulation or perception of pain is supported by the dense innervation of the periaqueductal grey (PAG) by MCH-positive fibers. Finally, MCH may participate in the regulation of fluid intake. ICV infusion of MCH in conscious sheep produced diuretic, natriuretic, and kaliuretic changes in response to increased plasma volume; Parkes, J. Neuroendocrinol. 8:57-63, (1996). Together with anatomical data reporting the presence of MCH in fluid regulatory areas of the brain, the results indicate that MCH may be an important peptide involved in the central control of fluid homeostasis in mammals.

In a recent citation MCHR1 antagonists surprisingly demonstrated their use as an anti-depressants and/or anti-anxiety agents. MCHR1 antagonists have been reported to show antidepressant and anxiolytic activities in rodent models, such as, social interaction, forced swimming test and ultrasonic vocalization. Therefore, MCHR1 antagonists could be useful to independently treat subjects with depression and/or anxiety. Also, MCHR1 antagonists could be useful to treat subjects that suffer from depression and/or anxiety and obesity.

This invention provides a method of treating an abnormality in a subject wherein the abnormality is alleviated by decreasing the activity of a mammalian MCH1 receptor which comprises administering to the subject an amount of a compound which is a mammalian MCH1 receptor antagonist effective to treat the abnormality. In separate embodiments, the abnormality is a regulation of a steroid or pituitary hormone disorder, an epinephrine release disorder, an anxiety disorder, genta gastrointestinal disorder, a cardiovascular disorder, an electrolyte balance disorder, hypertension, diabetes, a respiratory disorder, asthma, a reproductive function disorder, an immune disorder, an endocrine disorder, a musculoskeletal disorder, a neuroendocrine disorder, a cognitive disorder, a memory disorder, a sensory modulation and transmission disorder, a motor coordination disorder, a sensory integration disorder, a motor integration disorder, a dopaminergic function disorder, a sensory transmission disorder, an olfaction disorder, a sympathetic innervation disorder, an affective disorder, a stress-related disorder, a fluid-balance disorder, a seizure disorder,

pain, psychotic behavior, morphine tolerance, opiate addiction or migraine.

Compositions of the invention may conveniently be administered in unit dosage form and may be prepared by any of the methods well known in the pharmaceutical art, for example, as described in *Remington's Pharmaceutical Sciences* (Mack Pub. Co., Easton, PA, 1980).

The compounds of the invention can be employed as the sole active agent in a pharmaceutical or can be used in combination with other active ingredients which could facilitate the therapeutic effect of the compound.

Compounds of the present invention or a solvate or physiologically functional derivative thereof can be used as active ingredients in pharmaceutical compositions, specifically as a MCH receptor antagonists. By the term "active ingredient" is defined in the context of a "pharmaceutical composition" and shall mean a component of a pharmaceutical composition that provides the primary pharmaceutical benefit, as opposed to an "inactive ingredient" which would generally be recognized as providing no pharmaceutical benefit. The term "pharmaceutical composition" shall mean a composition comprising at one active ingredient and at least one ingredient that is not an active ingredient (for example and not limitation, a filler, dye, or a mechanism for slow release), whereby the composition is amenable to use for a specified, efficacious outcome in a mammal (for example, and not limitation, a human).

Pharmaceutical compositions, including, but not limited to, pharmaceutical compositions, comprising at least one compound of the present invention and/or an acceptable salt or solvate thereof (*e.g.*, a pharmaceutically acceptable salt or solvate) as an active ingredient combined with at least one carrier or excipient (*e.g.*, pharmaceutical carrier or excipient) may be used in the treatment of clinical conditions for which a MCH receptor antagonist is indicated. At least one compound of the present invention may be combined with the carrier in either solid or liquid form in a unit dose formulation. The pharmaceutical carrier must be compatible with the other ingredients in the composition and must be tolerated by the individual recipient. Other physiologically active ingredients may be incorporated into the pharmaceutical composition of the invention if desired, and if such ingredients are compatible with the other ingredients in the composition. Formulations may be prepared by any suitable method, typically by uniformly mixing the active compound(s) with liquids or finely divided solid carriers, or both, in the required proportions, and then, if

necessary, forming the resulting mixture into a desired shape.

Conventional excipients, such as binding agents, fillers, acceptable wetting agents, tabletting lubricants, and disintegrants may be used in tablets and capsules for oral administration. Liquid preparations for oral administration may be in the form of solutions, emulsions, aqueous or oily suspensions, and syrups. Alternatively, the oral preparations may be in the form of dry powder that can be reconstituted with water or another suitable liquid vehicle before use. Additional additives such as suspending or emulsifying agents, non-aqueous vehicles (including edible oils), preservatives, and flavorings and colorants may be added to the liquid preparations. Parenteral dosage forms may be prepared by dissolving the compound of the invention in a suitable liquid vehicle and filter sterilizing the solution before filling and sealing an appropriate vial or ampoule. These are just a few examples of the many appropriate methods well known in the art for preparing dosage forms.

It is noted that when the MCH receptor antagonists are utilized as active ingredients in a pharmaceutical composition, these are not intended for use only in humans, but in other non-human mammals as well. Indeed, recent advances in the area of animal health-care mandate that consideration be given for the use of MCH receptor antagonists for the treatment of obesity in domestic animals (*e.g.*, cats and dogs), and MCH receptor antagonists in other domestic animals where no disease or disorder is evident (*e.g.*, food-oriented animals such as cows, chickens, fish, etc.). Those of ordinary skill in the art are readily credited with understanding the utility of such compounds in such settings.

Pharmaceutically acceptable salts of the compounds of the invention can be prepared by reacting the free acid or base forms of these compounds with the appropriate base or acid in water, in an organic solvent, or in a mixture of the two; generally, nonaqueous media like ether, ethyl acetate, ethanol, isopropanol, dioxane, or acetonitrile are preferred. For instance, when the compound (I) possesses an acidic functional group, it can form an inorganic salt such as an alkali metal salt (e.g., sodium salt, potassium salt, etc.), an alkaline earth metal salt (e.g. calcium salt, magnesium salt, barium salt, etc.), and an ammonium salt. When the compound (I) possesses a basic functional group, it can form an inorganic salt (e.g., hydrochloride, sulfate, phosphate, hydrobromate, etc.) or an organic salt (e.g., acetate, maleate, fumarate, succinate, methanesulfonate, p-toluenesulfonate, citrate, tartrate, etc.).

When a compound of the invention contains optical isomers, stereoisomers, regio isomers, rotational isomers, a single substance and a mixture of them are included as a

compound of the invention. For example, when a chemical formula is represented as showing no stereochemical designation(s), such as Formula IX, then all possible stereoisomer, optical isomers and mixtures thereof are considered within the scope of that formula. Accordingly, Formula XXII, specifically designates the cis relationship between the two amino groups on the cyclohexyl ring and therefore this formula is also fully embraced by Formula IX.

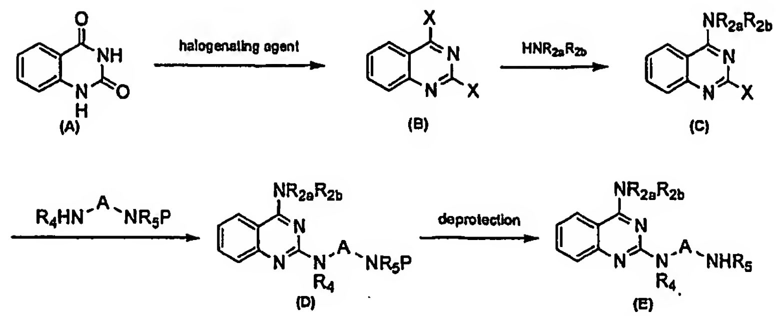
The novel substituted quinazolines of the present invention can be readily prepared according to a variety of synthetic manipulations, all of which would be familiar to one skilled in the art. Preferred methods for the preparation of compounds of the present invention include, but are not limited to, those described in Scheme 1-31.

The common intermediate (E) of the novel substituted quinazolines can be prepared as shown in Scheme 1. Commercially available 1*H*,3*H*-quinazoline-2,4-dione (A) is converted to 2,4-dihalo-quinazoline (B) by a halogenating agent with or without a base (wherein X is halogen such as chloro, bromo, or iodo). The halogenating agent includes phosphorous oxychloride ($POCl_3$), phosphorous oxybromide ($POBr_3$), or phosphorus pentachloride (PCl_5). The base includes a tertiary amine (preferably *N*,*N*-diisopropylethylamine, etc.) or an aromatic amine (preferably *N*,*N*-dimethylaniline, etc.). Reaction temperature ranges from about 100°C to 200°C, preferably about 140°C to 180°C. The halogen of 4-position of 2,4-dihalo-quinazoline (B) is selectively substituted by a primary or secondary amine ($HNR_{2a}R_{2b}$, wherein R_{2a} and R_{2b} are as defined above) with or without a base in an inert solvent to provide the corresponding 4-substitued amino adduct (C). The base includes an alkali metal carbonate (preferably sodium carbonate or potassium carbonate, etc.), an alkali metal hydroxide (preferably sodium hydroxide, etc.), or a tertiary amine (preferably *N*,*N*-diisopropylethylamine, triethylamine, or *N*-methylmorpholine, etc.). The inert solvent includes lower alkyl alcohol solvents (preferably methanol, ethanol, 2-propanol, or butanol, etc.), ethereal solvents (preferably tetrahydrofuran or dioxane, etc.), or amide solvents (preferably *N*,*N*-dimethylformamide or 1-methyl-pyrrolidin-2-one, etc.). Reaction temperature ranges from about 0°C to 200°C, preferably about 10°C to 150°C.

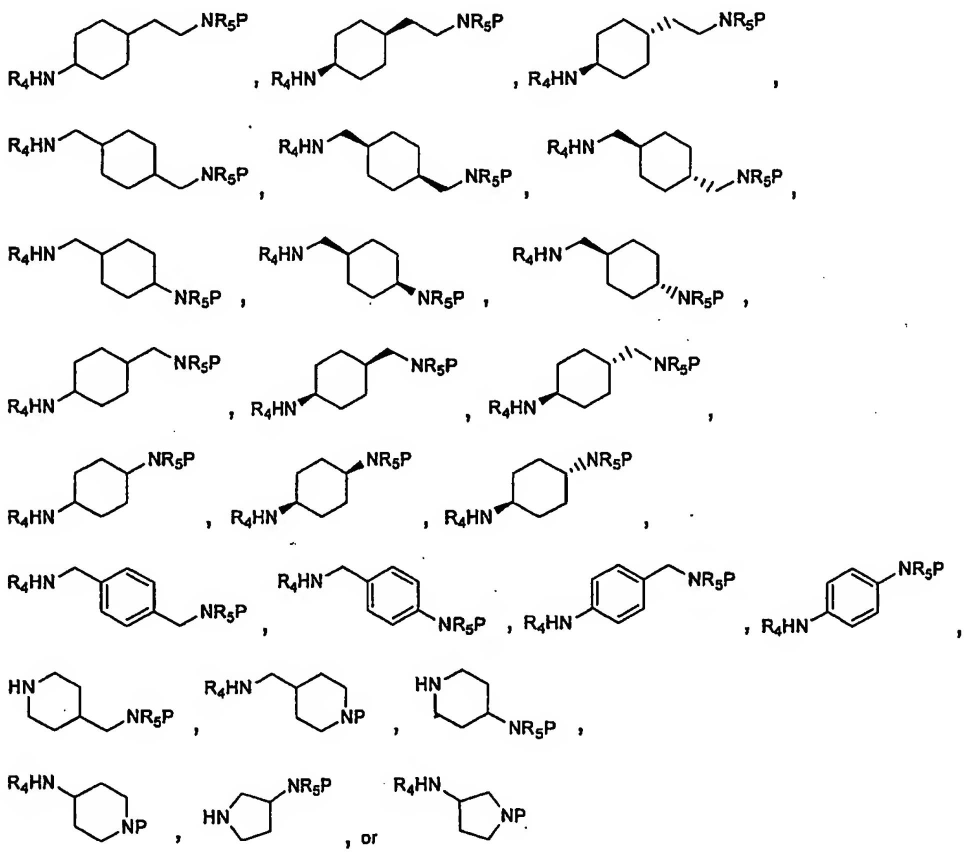
In turn, this is substituted by the mono-protected diamine (R_4HN-A-NR_5P, wherein R_4HN-A-NR_5P is as defined below, R_4 and R_5 are as defined above, and P is a protective group) with or without a base in an inert solvent to provide 2,4-disubstituted amino quinazoline (D). The base includes an alkali metal carbonate (preferably sodium carbonate

or potassium carbonate, etc.), an alkali metal hydroxide (preferably sodium hydroxide, etc.), or a tertiary amine (preferably *N,N*-diisopropylethylamine, triethylamine, or *N*-methylmorpholine, etc.). The inert solvent includes lower alkyl alcohol solvents (preferably methanol, ethanol, 2-propanol, or butanol, etc.) or amide solvents (preferably *N,N*-dimethylformamide or 1-methyl-pyrrolidin-2-one, etc.). Reaction temperature ranges from about 50°C to 200°C, preferably about 80°C to 150°C. Also this reaction can be carried out under microwave conditions. Representative protecting groups suitable for a wide variety of synthetic transformations are disclosed in Greene and Wuts, *Protective Groups in Organic Synthesis*, second edition, John Wiley & Sons, New York, 1991, the disclosure of which is incorporated herein by reference in its entirety. The deprotection of the protective group leads to the common intermediate (E) of the novel substituted quinazolines.

Scheme 1



$R_4HN{-}A{-}NR_5P$ is ;



The conversion of the common intermediate (E) to the novel substituted quinazolines (F-H) of the present invention is outlined in Scheme 2.

The amine (E) is reacted with a sulfonyl chloride (R_1SO_2Cl) and a base in an inert solvent to provide the novel sulfonamide (F) of the present invention. The base includes an alkali metal carbonate (preferably sodium carbonate or potassium carbonate, etc.), an alkali metal hydrogencarbonate (preferably sodium hydrogencarbonate or potassium hydrogencarbonate, etc.), an alkali hydroxide (preferably sodium hydroxide or potassium hydroxide, etc.), a tertiary amine (preferably *N,N*-diisopropylethylamine, triethylamine, or *N*-methylmorpholine, etc.), or an aromatic amine (preferably pyridine or imidazole, etc.). The inert solvent includes lower halocarbon solvents (preferably dichloromethane, dichloroethane, or chloroform, etc.), ethereal solvents (preferably tetrahydrofuran or dioxane), alcohol solvents (preferably 2-propanol, etc.), or aromatic solvents (preferably toluene or pyridine, etc.). Reaction temperature ranges from about -20°C to 50°C, preferably about 0°C to 40°C.

The amine (E) is reacted with a carboxylic acid (R_1CO_2H) and a dehydrating condensing agent in an inert solvent with or without a base to provide the novel amide (G) of the present invention. The dehydrating condensing agent includes dicyclohexylcarbodiimide (DCC), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC•HCl), bromo-tris-pyrrolidino-phosnium hexafluorophosphate (PyBroP), *O*-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU), or 1-cyclohexyl-3-methylpolystyrene-carbodiimide. The base includes a tertiary amine (preferably *N,N*-diisopropylethylamine or triethylamine, etc.). The inert solvent includes lower halocarbon solvents (preferably dichloromethane, dichloroethane, or chloroform, etc.), ethereal solvents (preferably tetrahydrofuran or dioxane), nitrile solvents (preferably acetonitrile, etc.), or amide solvents (preferably *N,N*-dimethylformamide, etc.). In case of need, 1-hydroxybenzotriazole (HOBT), HOBT-6-carboxaamidomethyl polystyrene, or 1-hydroxy-7-azabenzotriazole (HOAT) can be used as a reactant agent. Reaction temperature ranges from about -20°C to 50°C, preferably about 0°C to 40°C.

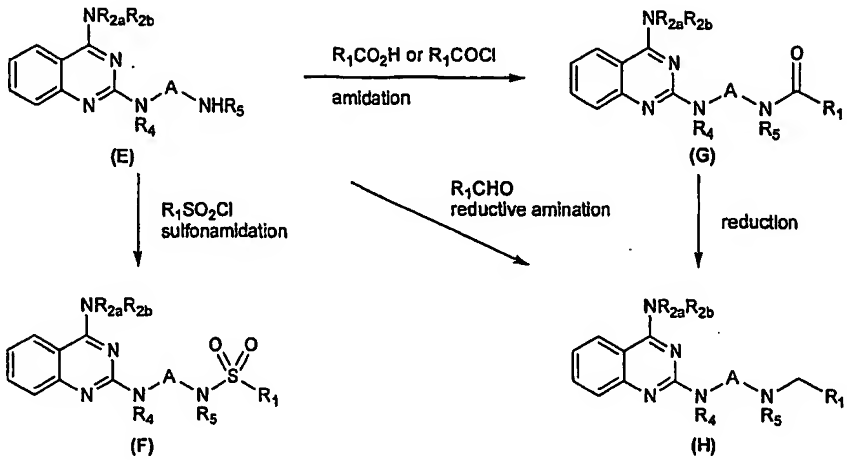
Alternatively, the novel amide (G) of the present invention can be obtained by amidation reaction using an acid chloride (R_1COCl) and a base in an inert solvent. The base includes an alkali metal carbonate (preferably sodium carbonate or potassium carbonate, etc.), an alkali metal hydrogencarbonate (preferably sodium hydrogencarbonate or

potassium hydrogencarbonate, etc.), an alkali hydroxide (preferably sodium hydroxide or potassium hydroxide, etc.), a tertiary amine (preferably *N,N*-diisopropylethylamine, triethylamine, or *N*-methylmorpholine, etc.), or an aromatic amine (preferably pyridine, imidazole, poly-(4-vinylpyridine), etc.). The inert solvent includes lower halocarbon solvents (preferably dichloromethane, dichloroethane, or chloroform, etc.), ethereal solvents (preferably tetrahydrofuran or dioxane), amide solvents (preferably *N,N*-dimethylformamide, etc.), or aromatic solvents (preferably toluene or pyridine, etc.). Reaction temperature ranges from about -20°C to 50°C, preferably about 0°C to 40°C.

The novel amide (G) of the present invention is reacted with a reducing agent in an inert solvent to provide the novel amine (H) of the present invention. The reducing agent includes alkali metal aluminum hydrides (preferably lithium aluminum hydride), alkali metal borohydrides (preferably lithium borohydride), alkali metal trialkoxyaluminum hydrides (preferably lithium tri-*tert*-butoxyaluminum hydride), dialkylaluminum hydrides (preferably di-isobutylaluminum hydride), borane, dialkylboranes (preferably di-isoamyl borane), alkali metal trialkylboron hydrides (preferably lithium triethylboron hydride). The inert solvent includes ethereal solvents (preferably tetrahydrofuran or dioxane) or aromatic solvents (preferably toluene, etc.). Reaction temperature ranges from about -78°C to 200°C, preferably about 50°C to 120°C.

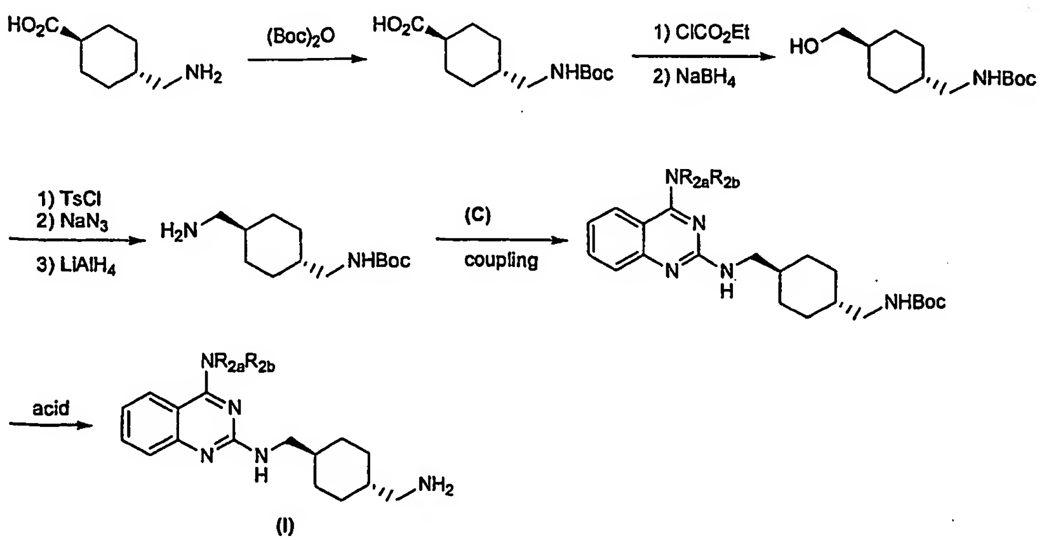
Alternatively, the novel amine (H) of the present invention can be obtained by reductive amination reaction using aldehyde (R_1CHO) and a reducing agent in an inert solvent with or without an acid. The reducing agent includes sodium triacetoxyborohydride, sodium cyanoborohydride, sodium borohydride, or boran-pyridine complex, preferably sodium triacetoxyborohydride or sodium cyanoborohydride. The inert solvent includes lower alkyl alcohol solvents (preferably methanol or ethanol, etc.), lower halocarbon solvents (preferably dichloromethane, dichloroethane, or chloroform, etc.), ethereal solvents (preferably tetrahydrofuran or dioxane), or aromatic solvents (preferably toluene, etc.). The acid includes an inorganic acid (preferably hydrochloric acid or sulfuric acid) or an organic acid (preferably acetic acid). Reaction temperature ranges from about -20°C to 120°C, preferably about 0°C to 100°C. Also this reaction can be carried out under microwave conditions.

Scheme 2



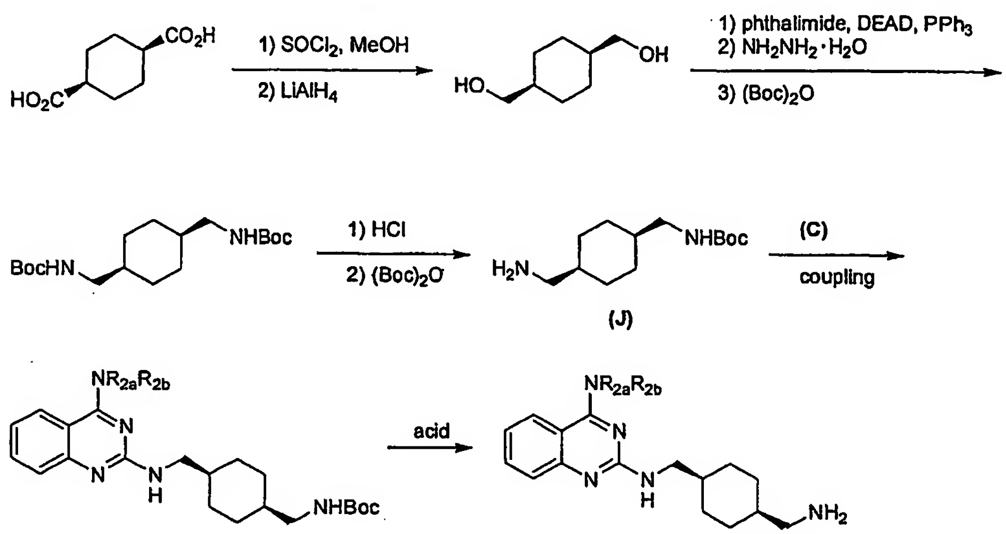
Compounds of Formula (I) can be prepared as shown in Scheme 3. The amine of commercially available *trans*-4-aminomethyl-cyclohexanecarboxylic acid is protected as *tert*-butyl carbamate. The carboxylic acid is reduced to the alcohol by sodium borohydride via the mixed acid anhydride. Tosylation of the alcohol with tosylchloride followed by azidation give the adide, which is converted to the amine by lithium aluminum hydride reduction. The coupling of the amine with the quinazoline core (C), which is synthesized in Scheme 1, gives 2,4-disubstituted amino quinazoline. The deprotection of Boc-group is achieved by an acid to give compounds of Formula (I).

Scheme 3



Compounds of Formula (K) can be prepared as shown in Scheme 4. Known *cis*-(4-aminomethyl-cyclohexylmethyl)-carbamic acid *tert*-butyl ester (J), synthesis of which is described in WO 01/72710, can be leaded to compounds of Formula (K) according to the method of scheme 3.

Scheme 4

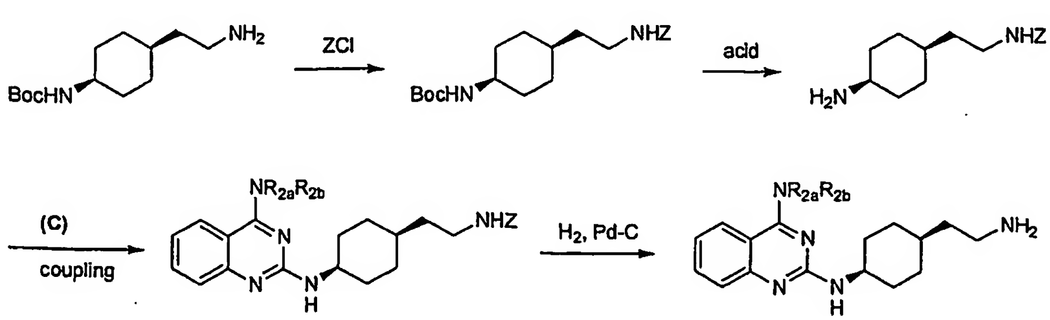


(J)

(K)

Compounds of Formula (L) can be prepared as shown in Scheme 5. The amine of *cis*-[4-(2-amino-ethyl)-cyclohexyl]-carbamic acid *tert*-butyl ester is protected as benzyl carbamate. The deprotection of Boc-group is achieved by an acid to give the amine. The coupling of the amine with quinazoline core (C), which is synthesized as scheme 1, gives 2,4-disubstituted amino quinazoline. The deprotection of Z-group is achieved by hydrogen reduction to give compounds of Formula (L).

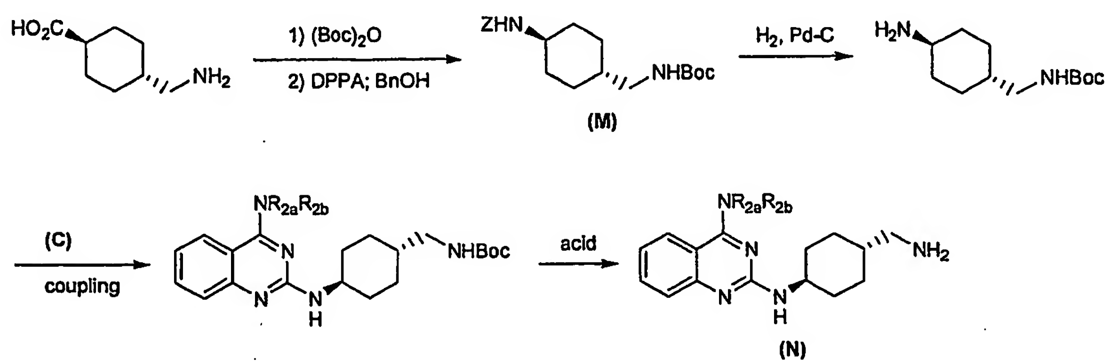
Scheme 5



(L)

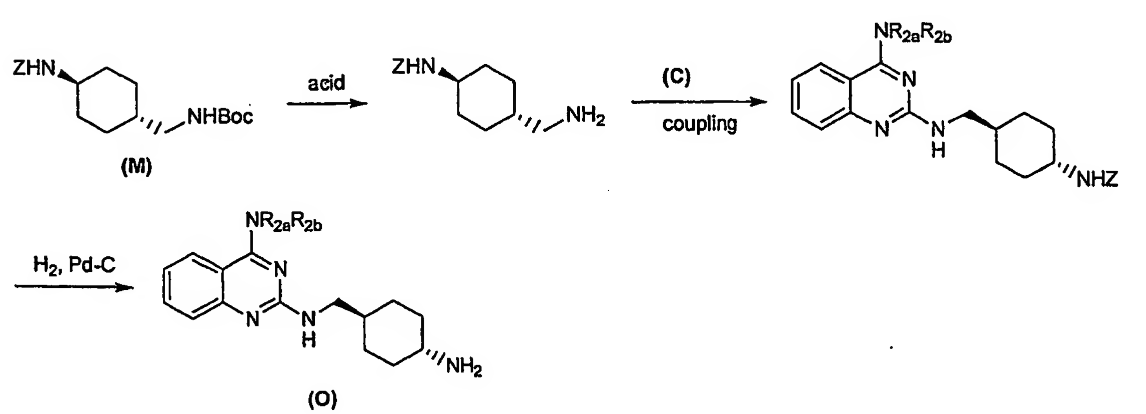
Compounds of Formula (N) can be prepared as shown in Scheme 6. The amine of commercially available *trans*-4-aminomethyl-cyclohexanecarboxylic acid is protected as *tert*-butyl carbamate. The carboxylic acid is transformed to benzyl carbamate (M) by curtius rearrangement. The deprotection of Z-group is achieved by hydrogen reduction to give the amine. The amine is converted to compounds of Formula (N) according to the method of scheme 3.

Scheme 6



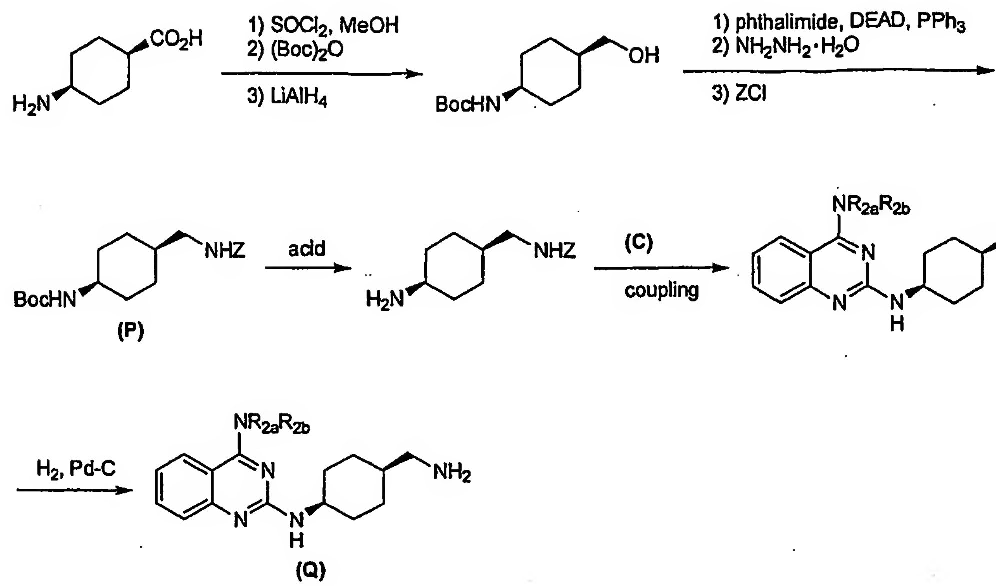
Compounds of Formula (O) can be prepared from the compound of Formula (M), which is described in Scheme 6, as shown in Scheme 7. The compound of Formula (M) can be leaded to compounds of Formula (O) according to the method of scheme 5.

Scheme 7



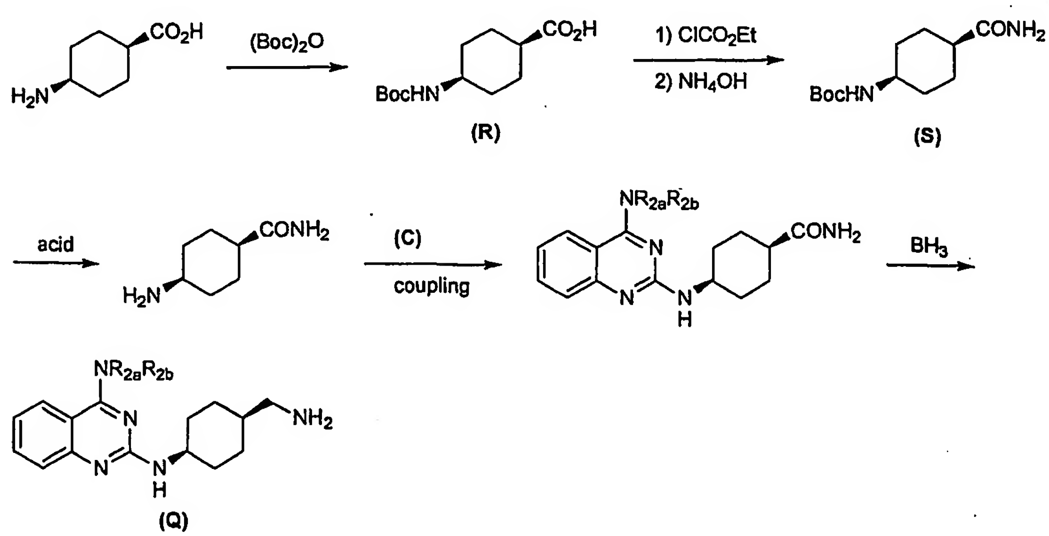
Compounds of Formula (Q) can be prepared as shown in Scheme 8. [4-(Benzyloxycarbonylamino-methyl)-cyclohexyl]-carbamic acid *tert*-butyl ester (P), synthesis of which is described in WO 01/72710, can be leaded to compounds of Formula (Q) according to the method of scheme 5.

Scheme 8



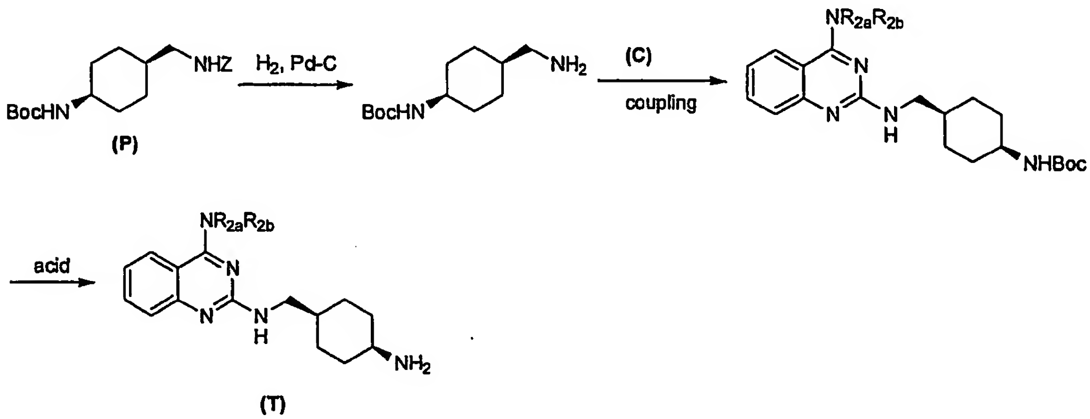
Alternatively compounds of Formula (Q) can be prepared as shown in Scheme 9. The amine of commercially available *cis*-4-amino-cyclohexanecarboxylic acid is protected as *tert*-butyl carbamate. The carboxylic acid (R) is converted to the amide (S) by aqueous ammonia via the mixed acid anhydride. The deprotection of Boc-group is achieved by an acid to give the amine. The coupling of the amine with quinazoline core (C), which is synthesized as scheme 1, gives 2,4-disubstituted amino quinazoline. The amide is reduced to compounds of Formula (Q).

Scheme 9



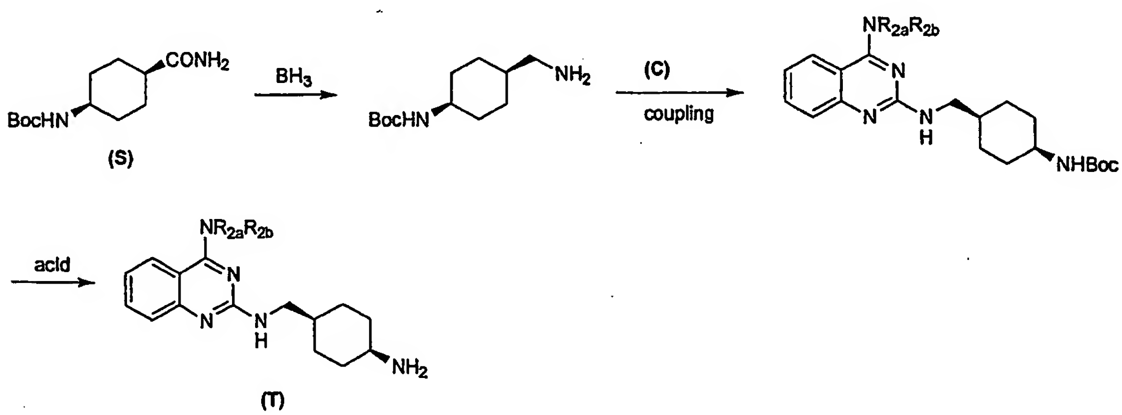
Compounds of Formula (T) can be prepared from the compound of Formula (P), which is described in Scheme 8, as shown in Scheme 10. The compound of Formula (P) can be leaded to compounds of Formula (T) according to the method of scheme 6.

Scheme 10



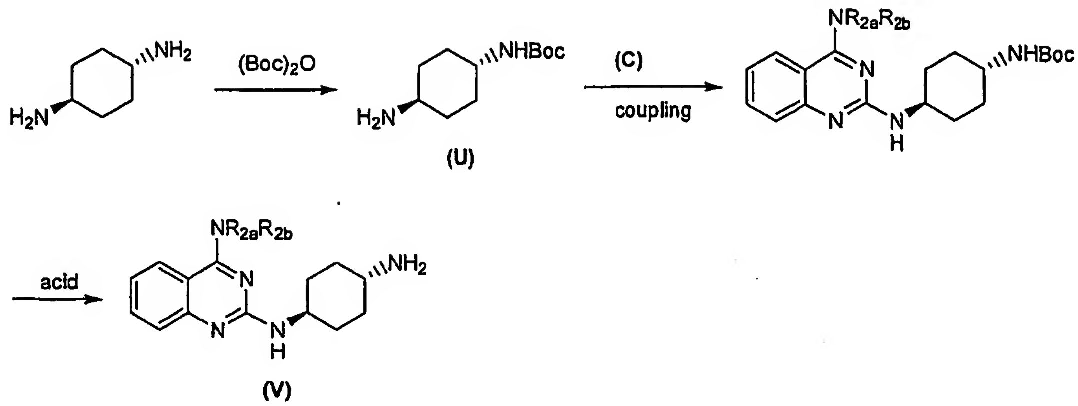
Alternatively compounds of Formula (T) can be prepared as shown in Scheme 11. The amide (S), which is described in Scheme 9, is reduced to the amine. The amine can be leaded to compounds of Formula (T) according to the method of scheme 3.

Scheme 11



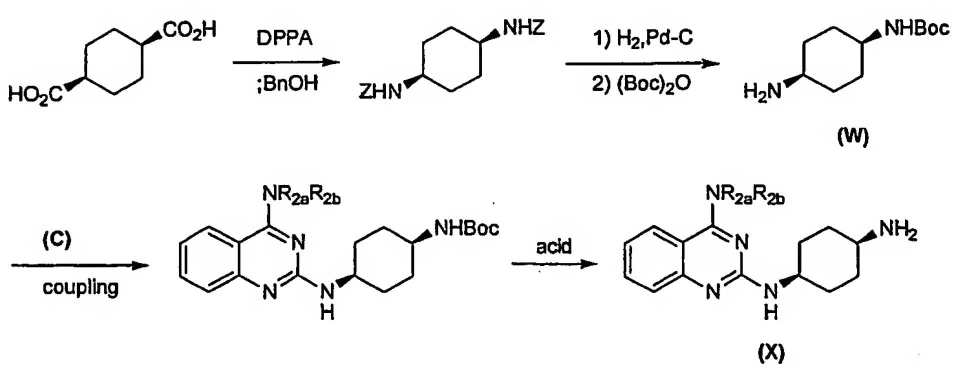
Compounds of Formula (V) can be prepared as shown in Scheme 12. The mono-protection of commercially available *trans*-cyclohexane-1,4-diamine can be achieved by the method described in *Synthetic communications*, **20**, 2559-2564 (1990). The conversion to compounds of Formula (V) can be accomplished according to the method of scheme 3.

Scheme 12



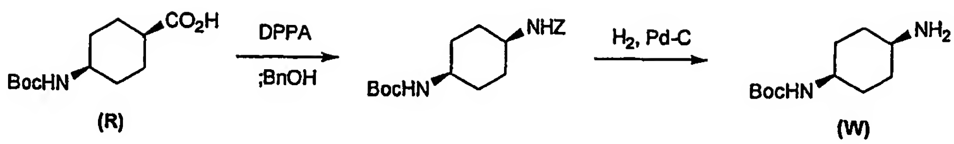
Compounds of Formula (X) can be prepared as shown in Scheme 13. The dicarboxylic acid of commercially available *cis*-cyclohexane-1,4-dicarboxylic acid is transformed to dibenzyl carbamate by curtius rearrangement. The deprotection of Z-group is achieved by hydrogen reduction to give the diamine. The mono-protection of the diamine can be achieved according to the method of scheme 12 to give the compound (W). The conversion to compounds of Formula (X) can be accomplished according to the method of scheme 3.

Scheme 13



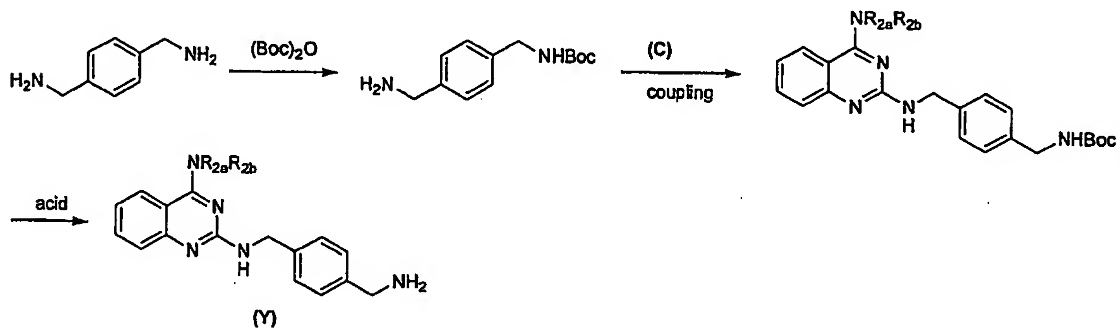
Alternatively the compound of Formula (W) can be prepared as shown in Scheme 14. The carboxylic acid (R), which is described in Scheme 9, is transformed to benzyl carbamate by curtius rearrangement. The deprotection of Z-group is achieved by hydrogen reduction to give the compound of Formula (W).

Scheme 14



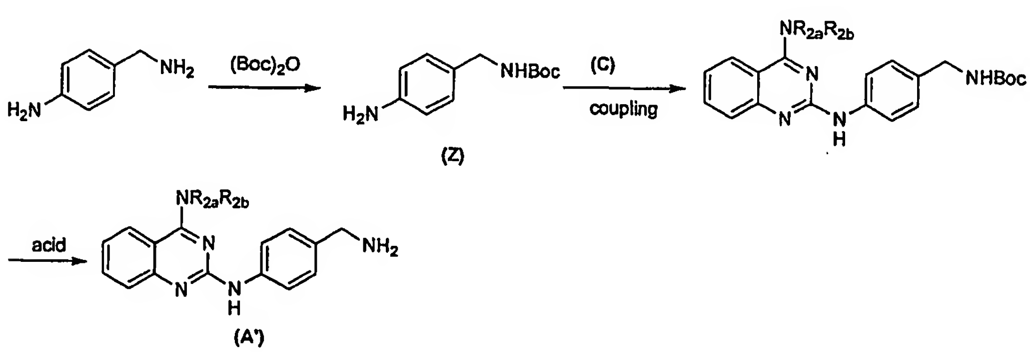
Compounds of Formula (Y) can be prepared according to the method described in Scheme 12 by using commercially available 4-aminomethyl-benzylamine as a starting material (Scheme 15).

Scheme 15



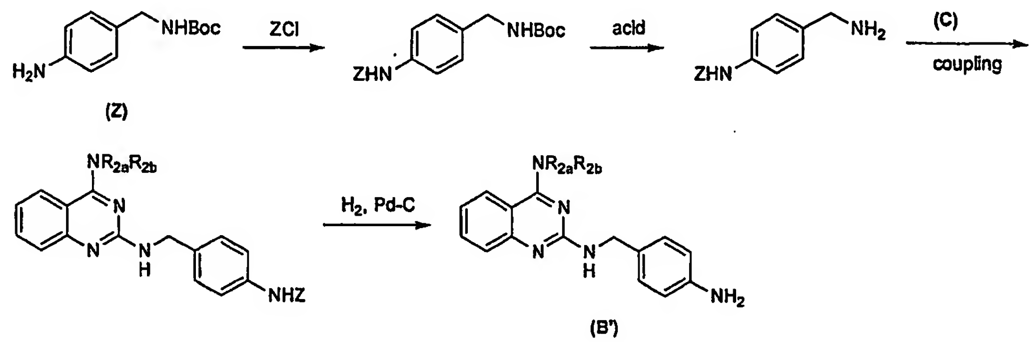
Compounds of Formula (A') can be prepared as shown in Scheme 16. The mono-protection of commercially available 4-aminomethyl-phenylamine can be achieved by using an equimolecular amount of $(Boc)_2O$ to give mono-*tert*-butyl carbamate (Z). The amine can be leaded to compounds of Formula (A') according to the method of scheme 3.

Scheme 16



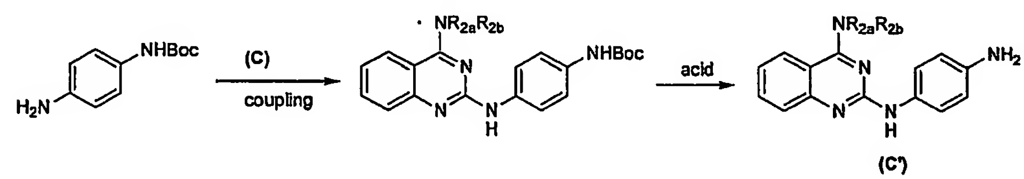
Compounds of Formula (B') can be prepared from the compound of Formula (Z), which is described in Scheme 16, as shown in Scheme 17. The compound of Formula (Z) can be leaded to compounds of Formula (B') according to the method of scheme 5.

Scheme 17



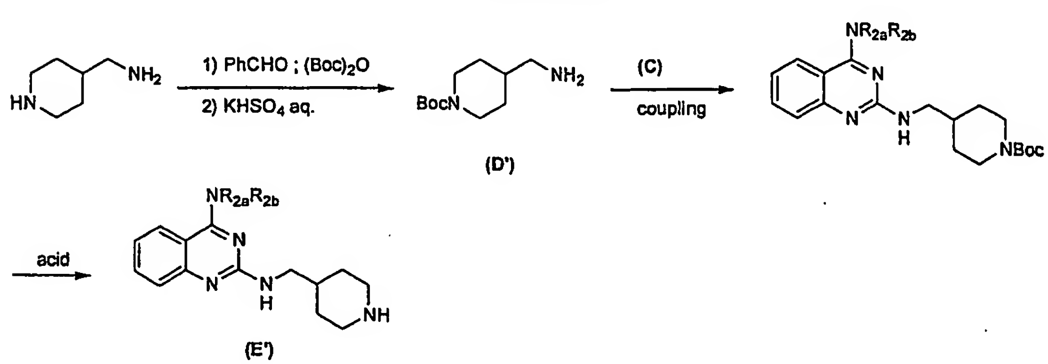
Compounds of Formula (C') can be prepared according to the method described in Scheme 3 by using commercially available (4-amino-phenyl)-carbamic acid *tert*-butyl ester as a starting material (Scheme 18).

Scheme 18



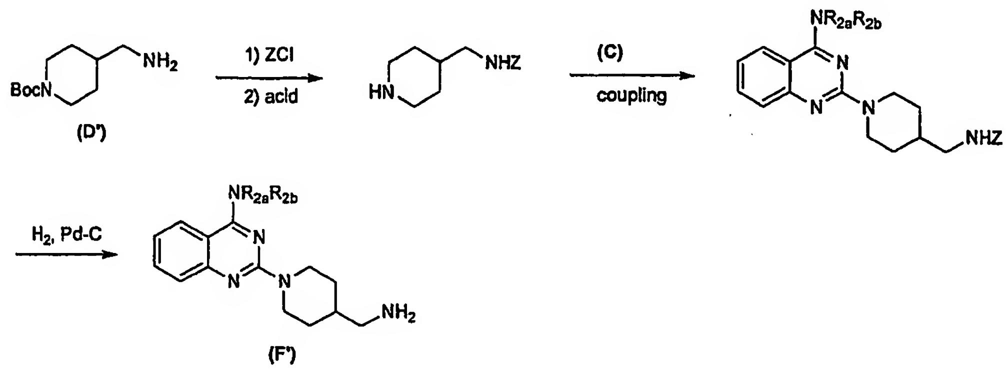
Compounds of Formula (E') can be prepared as shown in Scheme 19. The selective protection of the secondary amine in the presence of the primary amine of commercially available 4-(aminomethyl)piperidin is achieved by the method described in *Synthetic communications*, **22**, 2357-2360 (1992) to give the amine (D'). The amine is converted to compounds of Formula (E') according to the method of scheme 3.

Scheme 19



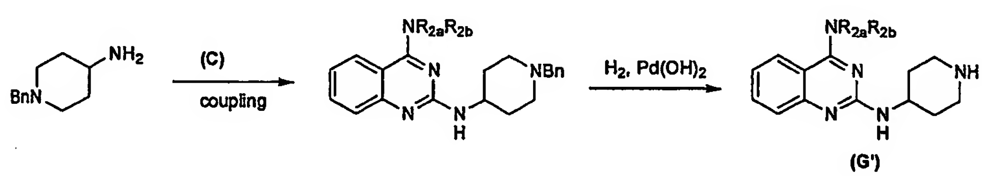
Compounds of Formula (F') can be prepared from the compound of Formula (D'), which is described in Scheme 19, as shown in Scheme 20. The compound of Formula (D') can be leaded to compounds of Formula (F') according to the method of Scheme 5.

Scheme 20



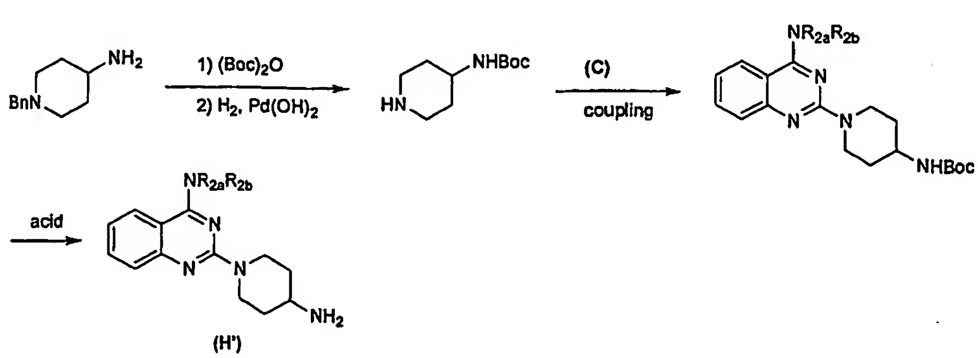
Compounds of Formula (G') can be prepared according to the method described in Scheme 5 by using commercially available 1-benzyl-piperidin-4-ylamine as a starting material (Scheme 21).

Scheme 21



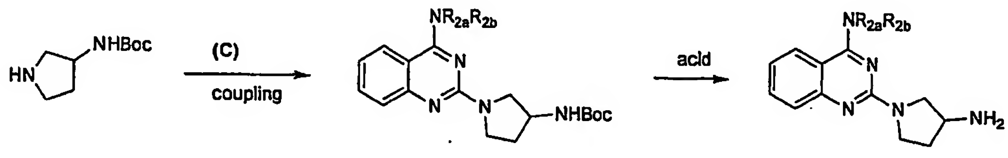
Compounds of Formula (H') can be prepared as shown in Scheme 22. The amine of commercially available 1-benzyl-piperidin-4-ylamine is protected as *tert*-butyl carbamate. The deprotection of benzyl group is achieved by hydrogen reduction to give the amine. The amine can be leaded to compounds of Formula (H') according to the method of scheme 3.

Scheme 22



Compounds of Formula (I') can be prepared according to the method described in Scheme 3 by using commercially available pyrrolidin-3-yl-carbamic acid *tert*-butyl ester as a starting material (Scheme 23).

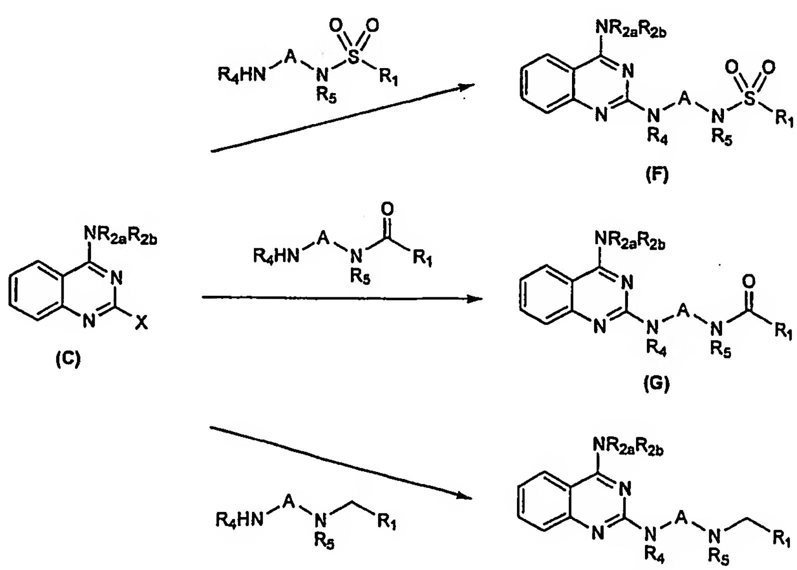
Scheme 23



(I')

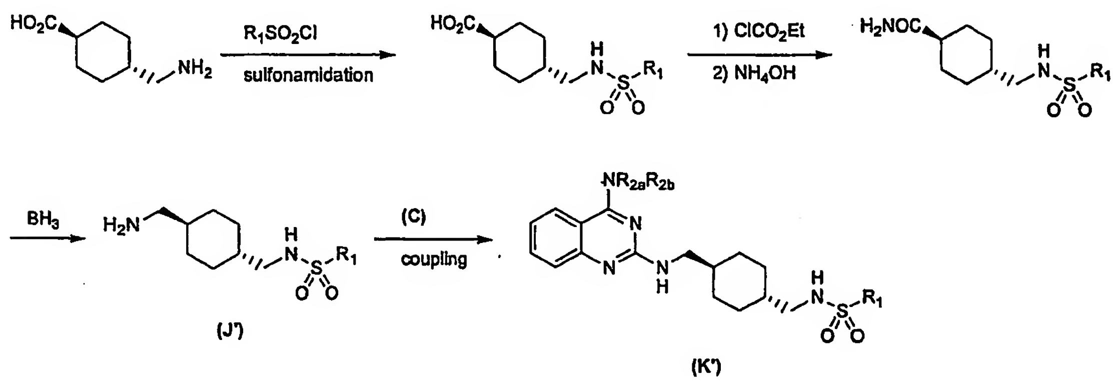
Alternatively, the novel sulfonamide (F), the novel amide (G), and the novel amine (H) of the present invention are directly synthesized from the quinazoline core (C), which is synthesized in Scheme 1, as shown in Scheme 24. This coupling is performed with or without a base in an inert solvent. The base includes an alkali metal carbonate (preferably sodium carbonate or potassium carbonate, etc.), an alkali metal hydroxide (preferably sodium hydroxide, etc.), or a tertiary amine (preferably *N,N*-diisopropylethylamine, triethylamine, or *N*-methylmorpholine, etc.). The inert solvent includes lower alkyl alcohol solvents (preferably methanol, ethanol, 2-propanol, or butanol, etc.) or amide solvents (preferably *N,N*-dimethylformamide or 1-methyl-pyrrolidin-2-one, etc.). Reaction temperature ranges from about 50°C to 200°C, preferably about 80°C to 180°C. Also this reaction can be carried out under microwave conditions.

Scheme 24



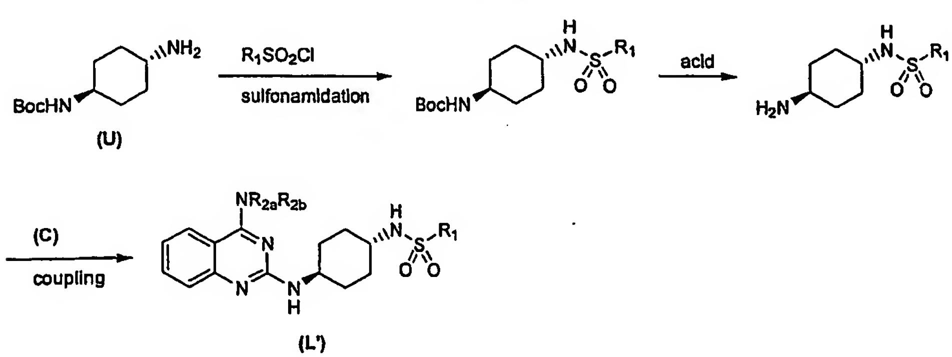
Compounds of Formula (K') can be prepared as shown in Scheme 25. Commercially available *trans*-4-aminomethyl-cyclohexanecarboxylic acid is reacted with sulfonyl chloride (R_1SO_2Cl) to give the sulfonamide. The carboxylic acid is converted to the amide via the mixed acid anhydride. The amide is reduced to the amine (J') by borane reduction. The coupling of the amine with the quinazoline core (C), which is synthesized in Scheme 1, gives the novel sulfonamide (K') of the present invention.

Scheme 25



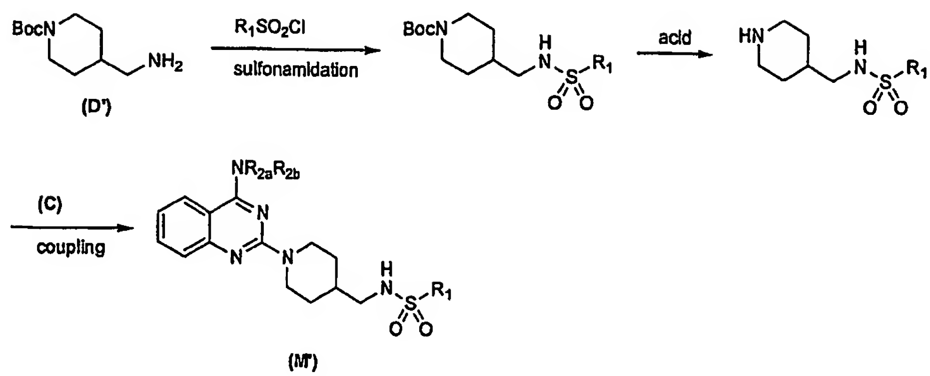
Compounds of Formula (L') can be prepared from the compound of Formula (U), which is described in Scheme 12, as shown in Scheme 26. The amine (U) is reacted with sulfonyl chloride (R_1SO_2Cl) to give the sulfonamide. The deprotection of Boc-group is achieved by an acid to give the amine. The coupling of the amine with quinazoline core (C), which is synthesized as scheme 1, gives the novel sulfonamide (L') of the present invention.

Scheme 26



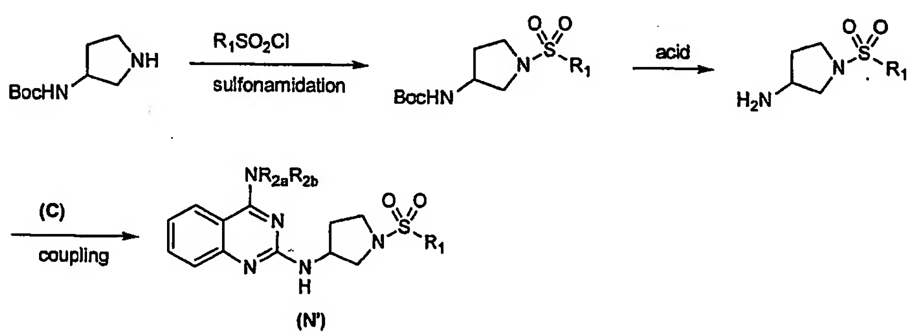
Compounds of Formula (M') can be prepared according to the method described in Scheme 26 by using the compound of Formula (D'), which is described in Scheme 19, as a starting material (Scheme 27).

Scheme 27



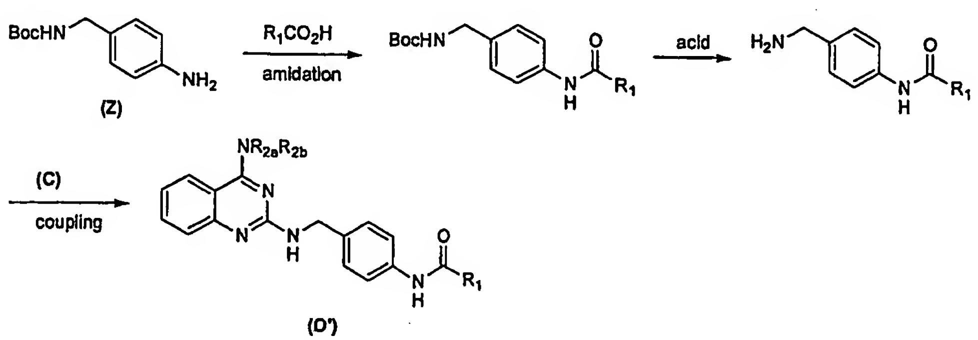
Compounds of Formula (N') can be prepared according to the method described in Scheme 26 by using commercially available pyrrolidin-3-yl-carbamic acid *tert*-butyl ester as a starting material (Scheme 28).

Scheme 28



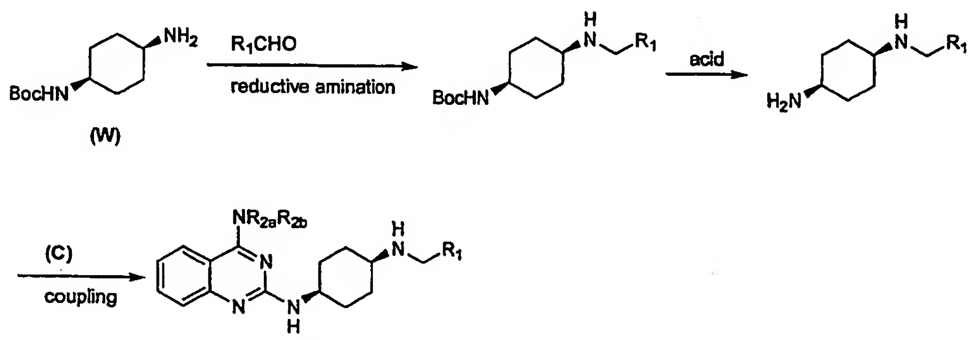
Compounds of Formula (O) can be prepared from the compound of Formula (Z), which is described in Scheme 16, as shown in Scheme 29. The aniline (Z) is reacted with carboxylic acid (R_1CO_2H) to give the amide. The deprotection of Boc-group is achieved by an acid to give the amine. The coupling of the amine with quinazoline core (C), which is synthesized as scheme 1, gives the novel sulfonamide (O') of the present invention.

Scheme 29



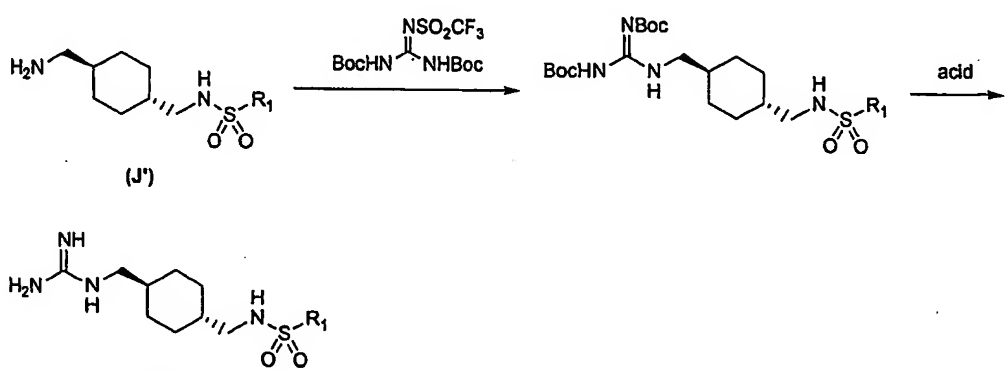
Compounds of Formula (P') can be prepared as shown in Scheme 30. The amine (W), which is synthesized in Scheme 13, is subjected to reductive amination by aldehyde (R_1CHO). The deprotection of Boc-group is achieved by an acid to give the amine. The coupling of the amine with quinazoline core (C), which is synthesized as scheme 1, gives the novel amine (P') of the present invention.

Scheme 30



Scheme 31 shows the preparation of compounds (Q') of the invention where Q of Formula I has Formula III. The compound (J'), which is synthesized in Scheme 25, is reacted with (1-*tert*-butoxycarbonylamino-1-trifluoromethanesulfonylimino-methyl)-carbamic acid *tert*-butyl ester. The deprotection of Boc-group is achieved by an acid to give the novel guanidine (Q') of the present invention.

Scheme 31



Examples

The compounds of the invention and their synthesis are further illustrated by the following examples. The following examples are provided to further define the invention without, however, limiting the invention to the particulas of these examples. "Ambient temperature" as referred to in the following example is meant to indicate a temperature falling between 0 °C and 40 °C.

Abbreviations used in the instant specification, particularly the Schemes and Examples, are as follows :

^{1}H NMR : proton nuclear magnetic resonance spectrum
AcOH : acetic acid
APCI : atmospheric pressure chemical ionization
$(Boc)_2O$: di-tertiary-butyl dicarbonate
BuLi : butyl lithium
BuOH : butanol
$CaCl_2$: calcium chloride
$CDCl_3$: deuterated chloroform
CF_3CO_2H : trifluoroacetic acid
CH_2Cl_2 : dichloromethane
$CHCl_3$: chloroform
CI : chemical ionization
CuCl : copper (I) chloride
D_2O : deuterium oxide
DMAP : 4-dimethylaminopyridine
DMF : *N,N*-dimethylformamide
DMSO : dimethyl sulfoxide
EDC : 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride
ESI : electrospray ionization
Et_2O : diethyl ether
EtOAc : acetic acid ethyl ester
EtOH : ethanol
FAB : fast atom bombardment
H_2SO_4 : sulfuric acid
HATU : *O*-(7-azabenzotriazol-1-yl)-*N,N,N',N'*-tetramethyluronium-

hexafluorophosphate

HCHO : formaldehyde

HCl : hydrogen chloride

HOAt : 1-hydroxy-7-azabenzotriazole

HOBt : 1-hydroxybenzotriazole

HPLC : high performance liquid chromatography

K_2CO_3 : potassium carbonate

$KHSO_4$: potassium bisulfate

Me_2NH : dimethylamine

$MeNH_2$: methylamine

MeOH : methanol

$MgSO_4$: magnesium sulfate

Na_2CO_3 : sodium carbonate

$Na_2SO_4 \cdot 10H_2O$: sodium sulfate decahydrate

$NaBH(OAc)_3$: sodium triacetoxyborohydride

$NaBH_3CN$: sodium cyanoborohydride

$NaBH_4$: sodium borohydride

$NaHCO_3$: sodium hydrogencarbonate

NaN_3 : sodium azide

$NaNO_2$: sodium nitrate

$Pd(OH)_2$: palladium hydroxide

Pd/C : palladium carbon

$POCl_3$: phosphoryl chloride

PVP : poly(4-vinylpyridine)

PyBroP : bromo-tris-pyrrolidino phosphonium hexafluoro phosphate

$SOCl_2$: thionyl chloride

t-BuOH : tertiary butanol

TFA : trifluoroacetic acid

THF : tetrahydrofuran

WSC : water solubule carbodiimide

ZCl : benzyloxycarbonyl chloride

s : singlet

d : doublet

t : triplet

q : qualtet

dd : doublet doublet

dt : doublet triplet

ddd : doublet doublet doublet

brs : broad singlet

m : multiplet

J : coupling constant

Hz : Hertz

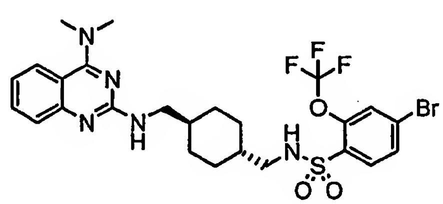
The analytical condition of high performance liquid chromatography is as follows:

Solvent A: 0.050% TFA in water

Solvent B: 0.035% TFA in acetonitrile

5 - 100% B over 5 min, flow rate 3.5 ml/min

Example 1



***trans*-4-Bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-2-trifluoromethoxy-benzenesulfonamide**

Step A: Synthesis of 2,4-dichloro-quinazoline.

To a suspension of 1*H*-quinazoline-2,4-dione (150 g, 925 mmol) in $POCl_3$ (549 mL, 5.89 mol) was added dimethyl-phenyl-amine (123 mL, 962 mmol). The mixture was stirred at reflux for 7 hr and concentrated. The solution was poured into ice water, and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (silica gel,

50% $CHCl_3$ in hexane to 10% EtOAc in $CHCl_3$) to give 2,4-dichloro-quinazoline (159g, 86%) as a pale yellow solid.

CI MS m/e 199, M^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27 (dt, J = 8.3, 1.1 Hz, 1 H), 7.95-8.04 (m, 2 H), 7.71-7.81 (m, 1 H).

Step B: Synthesis of (2-chloro-quinazolin-4-yl)-dimethyl-amine.

A solution of 2,4-dichloro-quinazoline (102 g, 530 mmol) in THF (1.2 L) was cooled to 4 °C and 50% aqueous Me_2NH (139 mL, 1.33 mol) was added. The mixture was stirred at ambient temperature for 80 min. The solution was alkalized with saturated aqueous $NaHCO_3$ (pH = 9), and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated. The residue was suspended in 50% Et_2O in hexane (250 mL) and stirred at ambient temperature for 30 min. The solid was collected by filtration, washed with 50% Et_2O in hexane, and dried at 80 °C to give (2-chloro-quinazolin-4-yl)-dimethyl-amine (104 g, 94%) as a pale yellow solid.

ESI MS m/e 207, M^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (d, J = 8.4 Hz, 1 H), 7.73-7.78 (m, 2 H), 7.68 (ddd, J = 8.4, 6.9, 1.4 Hz, 1 H), 3.41 (s, 6 H).

Step C: Synthesis of *trans*-4-(*tert*-butoxycarbonylamino-methyl)-cyclohexanecarboxylic acid.

To a solution of *trans*-4-aminomethyl-cyclohexanecarboxylic acid (150 g, 954 mmol) in 1.32 M aqueous sodium hydroxide (750 mL) were added *t*-BuOH (1680 mL) and $(Boc)_2O$ (215 g, 985 mmol). The reaction mixture was stirred at ambient temperature for 18 hr. To the reaction mixture was added H_2O (2.8 L), and cooled at 5 °C. The aqueous layer was acidified with saturated aqueous $KHSO_4$ (pH = 3), extracted with EtOAc (three times). The combined organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, concentrated and dried under reduced pressure to give *trans*-4-(*tert*-butoxycarbonylamino-methyl)-cyclohexanecarboxylic acid (165 g, 67%) as a white solid.

ESI MS m/e 280, M + Na^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.60 (brs, 1 H), 2.98 (t, J = 6.3 Hz, 2 H), 2.19-2.33 (m, 1 H), 1.99-2.11 (m, 2 H), 1.77-1.90 (m, 2 H), 1.44 (s, 9 H), 1.34-1.52 (m, 3 H), 0.86-1.05 (m, 2 H).

Step D: Synthesis of *trans*-(4-hydroxymethyl-cyclohexylmethyl)-carbamic acid *tert*-butyl ester.

A suspension of *trans*-4-(*tert*-butoxycarbonylamino-methyl)-cyclohexane-carboxylic acid (155 g, 603 mmol) in CH_2Cl_2 (1.35 L) was cooled at -65 °C and triethylamine (126 mL, 904 mmol) and a solution of ethyl chloroformate (58 mL, 751 mmol) in CH_2Cl_2 (200 mL) were added below -60 °C. The reaction mixture was stirred at 0 °C for 50 min. The mixture was acidified with saturated aqueous $KHSO_4$ (pH = 3), and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was washed with saturated aqueous Na_2CO_3 and brine, dried over $MgSO_4$, filtered, and concentrated to give a colorless oil. A solution of the above oil in THF (1.5 L) was cooled at -65 °C and $NaBH_4$ (26.6 g, 703 mmol) and MeOH (45 mL) were added. The mixture was stirred at -40 °C for 25 min, and stirred at 4 °C for 3 hr. The mixture was acidified with saturated aqueous $KHSO_4$ (pH = 3), and the aqueous layer was extracted with EtOAc (three times). The combined organic layer was washed with saturated aqueous Na_2CO_3 and brine, dried over $MgSO_4$, filtered, and concentrated, and purified by flash chromatography (silica gel, 17% MeOH in $CHCl_3$) to give *trans*-(4-hydroxymethyl-cyclohexylmethyl)-carbamic acid *tert*–butyl ester (123 g, 84%) as a white solid.

ESI MS m/e 266, M + Na^+; ^1H NMR (300 MHz, $CDCl_3$) δ 4.59 (brs, 1 H), 3.46 (d, J = 6.4 Hz, 2 H), 2.98 (t, J = 6.3 Hz, 2 H), 1.75-1.94 (m, 4 H), 1.45 (s, 9 H), 1.24-1.70 (m, 3 H), 0.81-1.12 (m, 4 H).

Step E: Synthesis of *trans*-(4-azidomethyl-cyclohexylmethyl)-carbamic acid *tert*-butyl ester.

A solution of *trans*-(4-hydroxymethyl-cyclohexylmethyl)-carbamic acid *tert*–butyl ester (123 g, 505 mmol) in pyridine (1 L) was cooled at 4 °C and a solution of *p*-toluenesulfonyl chloride (125 g, 657 mmol) in pyridine (200 ml) was added below 10 °C. The mixture was stirred at ambient temperature for 15 hr and concentrated. After dissolution with EtOAc and H_2O, the organic layer was separated. The aqueous layer was extracted with EtOAc (three times), the combined organic layer was washed with H_2O, dried over $MgSO_4$, filtered, and concentrated to give a pale yellow oil. To a solution of the above oil in DMF (1.6 L) was added NaN_3 (98.8 g, 1.52 mol). The reaction mixture was stirred at ambient temperature for 14 hr and concentrated. After dissolution with $CHCl_3$ and saturated aqueous $NaHCO_3$, the organic layer was separated. The aqueous layer was

extracted with $CHCl_3$ (three times), the combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (silica gel, 17% EtOAc in hexane) to give *trans*-(4-azidomethyl-cyclohexylmethyl)-carbamic acid *tert*-butyl ester (124 g, 91%) as a colorless oil.

ESI MS m/e 291, M + Na^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.59 (brs, 1 H), 3.13 (d, J = 6.5 Hz, 2 H), 2.98 (t, J = 6.4 Hz, 2 H), 1.70-1.90 (m, 4 H), 1.44 (s, 9 H), 1.25-1.65 (m, 2 H), 0.87-1.07 (m, 4 H).

Step F: Synthesis of *trans*-(4-aminomethyl-cyclohexylmethyl)-carbamic acid *tert*-butyl ester.

A suspension of lithium aluminum hydride (2.76 g, 72.6 mmol) in THF (225 mL) was cooled at 0 °C and a solution of *trans*-(4-azidomethyl-cyclohexylmethyl)-carbamic acid *tert*-butyl ester (15.0 g, 55.9 mmol) in THF (75 mL) was added over 1 hr. The reaction mixture was stirred at ambient temperature for 6 hr. The reaction was quenched with $Na_2SO_4 \cdot 10H_2O$, filtered through a pad of celite, and concentrated. The residue was purified by flash chromatography (silica gel, 50% MeOH in $CHCl_3$) to give *trans*-(4-aminomethyl-cyclohexylmethyl)-carbamic acid *tert*-butyl ester (12.3 g, 91%) as a pale yellow oil.

ESI MS m/e 243, M + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.60 (brs, 1 H), 2.97 (t, J = 6.3 Hz, 2 H), 2.53 (d, J = 6.4 Hz, 2 H), 1.70-1.92 (m, 4 H), 1.44 (s, 9 H), 1.08-1.54 (m, 4 H), 0.81-1.02 (m, 4 H).

Step G: Synthesis of *trans*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-carbamic acid *tert*-butyl ester.

A mixture of (2-chloro-quinazolin-4-yl)-dimethyl-amine (15.2 g, 73.3 mmol) and *trans*-(4-aminomethyl-cyclohexylmethyl)-carbamic acid *tert*-butyl ester (14.8 g, 61.0 mmol) in 2-propanol (80 mL) was stirred at reflux for 4 days, poured into saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica gel, 33% EtOAc in hexane) to give *trans*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-carbamic acid *tert*-butyl ester (20.4 g, 81%) as a pale yellow solid.

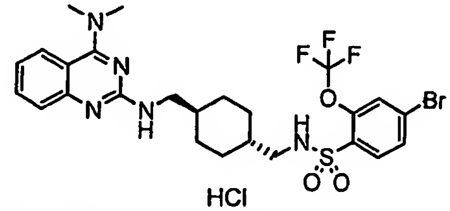
ESI MS m/e 414, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.2 Hz, 1 H), 7.40-7.52 (m, 2 H), 6.98-7.06 (m, 1 H), 4.93 (brs, 1 H), 4.59 (brs, 1 H), 3.35 (t, *J* = 6.2 Hz, 2 H), 3.26 (s, 6 H), 2.97 (t, *J* = 6.2 Hz, 2H), 1.72-1.95 (m, 4H), 1.44 (s, 9H), 1.30-1.62 (m, 2H), 0.84-1.12 (m, 4H).

Step H: Synthesis of *trans*-4-bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-2-trifluoromethoxy-benzenesulfonamide hydrochloride.

To a suspension of *trans*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]cyclohexylmethyl}-carbamic acid *tert*-butyl ester (3.84 g, 9.28 mmol) in EtOAc (50 mL) was added 4 M hydrogen chloride in EtOAc (38 mL). The mixture was stirred at ambient temperature for 40 min and concentrated to give a white solid. To a suspension of the solid in CH_2Cl_2 (50 mL) was added diisopropylethylamine (6.46 mL, 37.1 mmol). The mixture was cooled at 4 °C and a solution of 4-bromo-2-trifluoromethoxy-benzenesulfonyl chloride (3.31 g, 9.75 mmol) in CH_2Cl_2 (10 mL) was added below 5 °C. The reaction mixture was stirred at 4 °C for 1.5 hr. The reaction was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica gel, 20% EtOAc in hexane) to give *trans*-4-bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-2-trifluoromethoxy-benzenesulfonamide (3.45 g, 60%) as a pale yellow solid.

ESI MS m/e 616, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.9 Hz, 1 H), 7.81 (d, *J* = 7.6 Hz, 1 H), 7.35-7.61 (m, 4 H), 7.02 (t, *J* = 6.8 Hz, 1 H), 4.96 (brs, 1 H), 3.35 (t, *J* = 6.1 Hz, 2 H), 3.26 (s, 6 H), 2.79 (d, *J* = 6.7 Hz, 2 H), 1.32-1.98 (m, 6 H), 0.72-1.12 (m, 4 H).

Example 2



***trans*-4-Bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-**

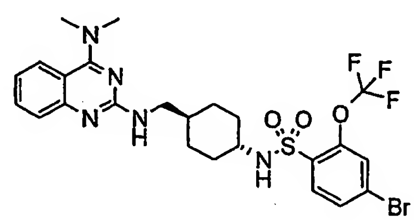
cyclohexylmethyl}-2-trifluoromethoxy-benzenesulfonamide hydrochloride

Step A: Synthesis of *trans*-4-bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-2-trifluoromethoxy-benzenesulfonamide hydrochloride.

A solution of *trans*-4-bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-2-trifluoromethoxy-benzenesulfonamide obtained step H of example 1 (3.45 g, 5.61 mmol) in EtOAc (100 mL) was cooled on an ice-bath and 4 M hydrogen chloride in EtOAc (1.66 mL) was added. The mixture was stirred at ambient temperature for 1 hr and concentrated to give a white solid. The solid was recrystallized from 16% EtOH in Et_2O, and dried under reduced pressure to give *trans*-4-bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-2-trifluoromethoxy-benzenesulfonamide hydrochloride (2.76g, 75%) as a white solid.

ESI MS m/e 616, M + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.50 (brs, 1H), 8.42 (t, J = 6.0 Hz, 1 H), 7.86-7.94 (m, 2 H), 7.51-7.68 (m, 4H), 7.21-7.28 (m, 1 H), 4.83 (d, J = 6.4 Hz, 1 H), 3.51 (s, 6 H), 3.35 (t, J = 6.0 Hz, 2H), 2.78 (t, J = 6.4 Hz, 2H), 1.73-1.95 (m, 4H), 1.35-1.65 (m, 2H), 0.81-1.12 (m, 4H).

Example 3



***trans*-4-Bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexyl}-2-trifluoromethoxy-benzenesulfonamide**

Step A: Synthesis of *trans*-[4-(*tert*-butoxycarbonylamino-methyl)-cyclohexyl]-carbamic acid benzyl ester.

To a suspension of *trans*-4-aminomethyl-cyclohexanecarboxylic acid (15.0 g, 95.4 mmol) in $CHCl_3$ (150 mL) were added 1 M aqueous sodium hydroxide (150 mL) and $(Boc)_2O$ (21.9 g, 100 mmol) successively. The reaction mixture was stirred at ambient

temperature for 15 hr, and partitioned between $CHCl_3$ and water. The aqueous layer was acidified with saturated aqueous $KHSO_4$ (pH = 3), extracted with $CHCl_3$ (three times). The combined organic layer was washed with brine, dried over $MgSO_4$, filtered, and concentrated to give a white solid. To a suspension of the above solid in benzene (75 mL) were added phosphorazidic acid diphenyl ester (16.2 g, 58.9 mmol) and triethylamine (5.94 g, 58.7 mmol). The reaction mixture was stirred at reflux for 3 hr (**Caution! Vigorous exothermic reaction**). Benzyl alcohol (6.65 g, 61.5 mmol) was added, the reaction mixture was stirred at reflux for 24 hr, concentrated. After dissolution with EtOAc and H_2O, the organic layer was separated. The aqueous layer was extracted with EtOAc (twice), the combined organic layer was washed with 1 M aqueous $KHSO_4$, saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (silica gel, 33% EtOAc in hexane) to give a white solid. A suspension of the above solid in Et_2O was stirred at ambient temperature for 30 min and filtered. The filtrate was washed with Et_2O and dried under reduced pressure to give *trans*-[4-(*tert*-butoxycarbonylamino-methyl)-cyclohexyl]-carbamic acid benzyl ester (17.4 g, 50%) as a white solid.

ESI MS m/e 385, M + Na^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22-7.41 (m, 5 H), 5.09 (s, 2 H), 4.20-4.68 (m, 2 H), 3.23-3.60 (m, 1 H), 2.96 (t, 2 H, J = 6.4 Hz), 1.62-2.18 (m, 4 H), 1.44 (s, 9 H), 1.30-1.60 (m, 1 H), 0.90-1.23 (m, 4 H).

Step B: Synthesis of *trans*-(4-aminomethyl-cyclohexyl)-carbamic acid benzyl ester hydrochloride.

To a suspension of *trans*-[4-(*tert*-butoxycarbonylamino-methyl)-cyclohexyl]-carbamic acid benzyl ester (4.00 g, 11.0 mmol) in EtOAc (40 mL) was added 4 M hydrogen chloride in EtOAc (10 mL). To the reaction mixture was added $CHCl_3$ (10 mL) and the mixture was stirred at ambient temperature for 3 hr. To the reaction mixture was 4 M hydrogen chloride in EtOAc (20 mL) and the mixture was stirred at ambient temperature for 1.5 hr, filtered, washed with EtOAc, and dried under reduced pressure to give *trans*-(4-aminomethyl-cyclohexyl)-carbamic acid benzyl ester hydrochloride (2.96 g, 90%) as a white solid.

ESI MS m/e 263, M (free) + H^+; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.12 (brs, 3 H), 7.25-7.40 (m, 5 H), 7.21 (d, 1 H, J = 7.8 Hz), 5.00 (s, 2 H), 3.17-3.30 (m, 1 H), 2.62 (d, 2 H, J = 7.0 Hz), 1.64-1.88 (m, 4 H), 1.42-1.60 (m, 1 H), 0.90-1.21 (m, 4 H).

Step C: Synthesis of *trans*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexyl}-carbamic acid benzyl ester.

A mixture of (2-chloro-quinazolin-4-yl)-dimethyl-amine (1.50 g, 7.22 mmol) and *trans*-(4-aminomethyl-cyclohexyl)-carbamic acid benzyl ester hydrochloride (2.59 g, 8.67 mmol) in 2-propanol (15 mL) was stirred at reflux for 8 days and dissolved in $CHCl_3$ and MeOH. The mixture was poured into saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica gel, 33% EtOAc in hexane) to give *trans*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexyl}-carbamic acid benzyl ester (1.20 g, 38%) as a pale yellow solid.

ESI MS m/e 434, $M + H^+$; ^1H NMR (300 MHz, $CDCl_3$) δ 7.76-7.82 (m, 1 H), 7.40-7.50 (m, 2 H), 7.25-7.40 (m, 5 H), 6.95-7.04 (m, 1 H), 5.08 (s, 2 H), 4.82-5.05 (m, 1 H), 4.40-4.70 (m, 1 H), 3.40-3.60 (m, 1 H), 3.35 (t, 2 H, J = 6.3 Hz), 3.26 (s, 6 H), 1.96-2.18 (m, 2 H), 1.80-1.96 (m, 2 H), 1.45-1.61 (m, 1 H), 1.00-1.20 (m, 4 H).

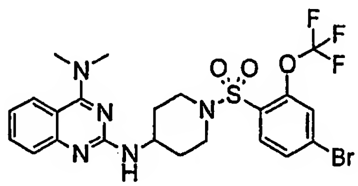
Step D: Synthesis of *trans*-4-bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexyl}-2-trifluoromethoxy-benzenesulfonamide.

To a suspension of *trans*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexyl}-carbamic acid benzyl ester (500 mg, 1.15 mmol) in MeOH (5 mL) was added 5% Pd/C (50 mg). The mixture was stirred at ambient temperature under hydrogen atmosphere for 2 hr, at 50 °C for 8 hr, and at ambient temperature for 10.5 hr, filtered, and concentrated to give a colorless oil. To a solution of the above oil in CH_2Cl_2 (5 mL) was added diisopropylethylamine (420 μL, 2.41 mmol). The mixture was cooled to 4 °C and a solution of 4-bromo-2-trifluoromethoxy-benzenesulfonyl chloride (431 mg, 1.27 mmol) in CH_2Cl_2 (2 mL) was added below 5 °C. The reaction mixture was stirred at 4 °C for 1.5 hr. The reaction was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica gel, 33% to 50% EtOAc in hexane) to give *trans*-4-bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexyl}-2-trifluoromethoxy-benzenesulfonamide (560 mg, 81%) as a pale yellow solid.

ESI MS m/e 602, $M + H^+$; ^1H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, 1 H, J = 8.9 Hz), 7.80

(dd, 1 H, $J = 8.4$, 0.9 Hz), 7.38-7.58 (m, 4 H), 7.01 (ddd, 1 H, $J = 8.4$, 6.7, 1.6 Hz), 4.85-5.04 (m, 1 H), 3.31 (t, 2 H, $J = 6.3$ Hz), 3.24 (s, 6 H), 3.07-3.20 (m, 1 H), 1.70-1.90 (m, 4 H), 1.42-1.58 (m, 1 H) , 0.90-1.28 (m, 4 H).

Example 4



N^2-[1-(4-Bromo-2-trifluoromethoxy-benzenesulfonyl)-piperidin-4-yl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine

Step A: Synthesis of N^2-(1-benzyl-piperidin-4-yl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine.

Using the procedure for the step G of example 1, the title compound was obtained. ESI MS m/e 362, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, $J = 7.6$ Hz, 1 H), 7.20-7.52 (m, 7 H), 6.97-7.05 (m, 1 H) , 4.74-4.90 (m, 1 H) , 3.90-4.05 (m, 1 H), 3.53 (s, 2 H), 3.26 (s, 6 H), 2.78-2.90 (m, 2 H), 2.02-2.24 (m, 4 H), 1.48-1.62 (m, 2 H).

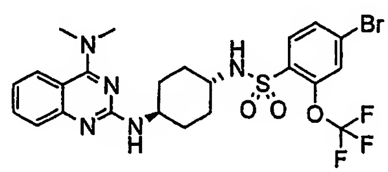
Step B: Synthesis of N^2-[1-(4-bromo-2-trifluoromethoxy-benzenesulfonyl)-piperidin-4-yl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine.

To a solution of N^2-(1-benzyl-piperidin-4-yl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine (500 mg, 1.38 mmol) in MeOH (5 mL) was added 20% $Pd(OH)_2$ (100 mg). The mixture was stirred at ambient temperature under hydrogen atmosphere for 1.5 hr, at 50 °C for 8 hr, at ambient temperature for 16.5 hr, filtered through a pad of celite, and concentrated. To a solution of the residue in CH_2Cl_2 (5 mL) was added diisopropylethylamine (510 μL, 2.93 mmol). The mixture was cooled to 4 °C and a solution of 4-bromo-2-trifluoromethoxy-benzenesulfonyl chloride (493 mg, 1.45 mmol) in CH_2Cl_2 (2 mL) was added below 5 °C. The reaction mixture was stirred at 4 °C for 2 hr. The reaction was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$,

filtered, concentrated, and purified by flash chromatography (NH-silica gel, 33% EtOAc in hexane) to give N^2-[1-(4-bromo-2-trifluoromethoxy-benzenesulfonyl)-piperidin-4-yl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine (339 mg, 43%) as a pale yellow solid.

ESI MS m/e 596, M + Na^+; ^1H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, J = 8.2 Hz, 1 H), 7.81 (dd, J = 8.3, 1.0 Hz, 1 H), 7.36-7.61 (m, 4 H), 7.04 (ddd, J = 8.3, 6.8, 1.4 Hz, 1 H), 4.77 (d, J = 7.8 Hz, 1 H), 3.97-4.14 (m, 1 H), 3.68-3.86 (m, 2 H), 3.25 (s, 6 H), 2.87-3.01 (m, 2 H), 2.10-2.23 (m, 2 H), 1.51-1.70 (m, 2 H).

Example 5



***trans*-4-Bromo-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-2-trifluoromethoxy-benzenesulfonamide**

Step A: Synthesis of *trans*-(4-amino-cyclohexyl)-carbamic acid *tert*-butyl ester.

To a solution of *trans*-cyclohexane-1,4-diamine (15.0 g, 131 mmol) in 1,4-dioxane (85 mL) was added $(Boc)_2O$ (3.61 g, 16.5 mmol) dropwise over 4 hr. The mixture was stirred at ambient temperature for 19 hr and concentrated. To the residue was added H_2O and the insoluble material was removed by filtration. The filtrate was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated to give *trans*-(4-amino-cyclohexyl)-carbamic acid *tert*-butyl ester (3.15 g, 11% based on diamine, 89% based on $(Boc)_2O$) as a white solid.

ESI MS m/e 215, M + H^+; ^1H NMR (300 MHz, $CDCl_3$) δ 4.43 (brs, 1 H), 3.36 (brs, 1 H), 2.57-2.70 (m, 1 H), 1.78-2.04 (m, 4 H), 1.44 (s, 9 H), 1.05-1.38 (m, 4 H).

Step B: Synthesis of *trans*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-carbamic acid *tert*-butyl ester.

Using the procedure for the step G of example 1, the title compound was obtained.

ESI MS m/e 408, M + Na^+; ^1H NMR (300 MHz, $CDCl_3$) δ 7.80 (d , J = 8.2 Hz, 1 H), 7.39-

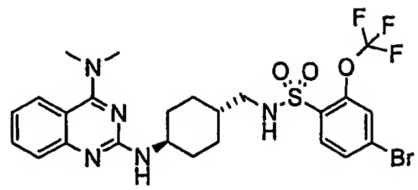
7.52 (m, 2 H), 7.02 (ddd, 1 H, J = 8.3, 6.3, 1.9 Hz, 1 H), 4.68-4.78 (m, 1 H), 4.43 (brs, 1 H), 3.89 (brs, 1 H), 3.46 (brs, 1 H), 3.25 (s, 6 H), 2.15-2.24 (m, 2 H), 1.97-2.10 (m, 2 H), 1.45 (s, 9 H), 1.21-1.35 (m, 4 H).

Step C: Synthesis of *trans*-4-bromo-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-2-trifluoromethoxy-benzenesulfonamide.

To a solution of *trans*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-carbamic acid *tert*-butyl ester (500 mg, 1.30 mmol) in EtOAc (5 mL) was added 4 M hydrogen chloride in EtOAc (5 mL). The mixture was stirred at ambient temperature for 1 hr and concentrated to give a white solid. To a suspension of the above solid in CH_2Cl_2 (7 mL) was added diisopropylethylamine (905 μL, 5.20 mmol). The mixture was cooled to 4 °C and a solution of 4-bromo-2-trifluoromethoxy-benzenesulfonyl chloride (462 mg, 1.36 mmol) in CH_2Cl_2 (2 mL) was added below 5 °C. The reaction mixture was stirred at 4 °C for 1.5 hr. To the reaction mixture was added a solution of 4-bromo-2-trifluoromethoxy-benzenesulfonyl chloride (88 mg, 0.26 mmol) in CH_2Cl_2 (0.5 mL) and the mixture was stirred at 4 °C for 1 hr. To the reaction mixture was added diisopropylethylamine (230 μL, 1.32 mmol) and the mixture was stirred at 4 °C for 1.5 hr. The reaction was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica gel, 50% EtOAc in hexane) to give *trans*-4-bromo-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-2-trifluoromethoxy-benzenesulfonamid (339 mg, 44%) as a white solid.

ESI MS m/e 588, M + H^+; ^1H NMR (300 MHz, $CDCl_3$) δ 7.92 (d , J = 8.9 Hz, 1 H), 7.80 (dd , J = 8.3, 0.7 Hz, 1 H), 7.37-7.59 (m, 4 H), 6.99-7.06 (m, 1 H), 4.64-4.75 (m, 1 H), 3.78-3.94 (m, 1 H), 3.17-3.30 (m, 7 H), 2.09-2.20 (m, 2 H), 1.85-1.97 (m, 2 H), 1.12-1.47 (m, 4 H).

Example 6



***trans*-4-Bromo-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-trifluoromethoxy-benzenesulfonamide**

Step A: Synthesis of *trans*-(4-amino-cyclohexylmethyl)-carbamic acid *tert*-butyl ester.

To a suspension of *trans*-[4-(*tert*-butoxycarbonylamino-methyl)-cyclohexyl]-carbamic acid benzyl ester (4.00 g, 11.0 mmol) in MeOH (40 mL) was added 5% Pd/C (400 mg). The mixture was stirred at ambient temperature under hydrogen atmosphere for 1 hr, filtered through a pad of celite, and concentrated to give a white solid. A suspension of the above solid in hexane (15 mL) was stirred at ambient temperature for 30 min. The solid was collected by filtration, washed with hexane, dried under reduced pressure to give *trans*-(4-amino-cyclohexylmethyl)-carbamic acid *tert*-butyl ester (2.52 g, 100%) as a white solid.

ESI MS m/e 229, M + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.56-4.88 (m, 1 H), 3.00 (t, J = 6.5 Hz, 2 H), 2.54-2.65 (m, 1 H), 1.70-1.94 (m, 4 H), 1.44 (s, 9 H), 1.18-1.50 (m, 1 H), 0.92-1.15 (m, 4 H).

Step B: Synthesis of *trans*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-carbamic acid *tert*-butyl ester.

Using the procedure for the step G of example 1, the title compound was obtained.

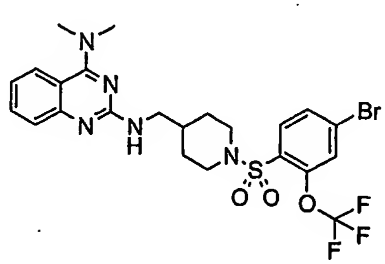
ESI MS m/e 422, M + Na^+; ^{1}H NMR (300 MHz, $CDCl_3$) 7.81 (d, J = 7.9 Hz, 1 H), 7.38-7.52 (m, 2 H) , 6.96-7.07 (m, 1 H), 4.55-4.84 (m, 2 H), 3.75-3.97 (m, 1 H), 3.26 (s, 6 H), 3.01 (t, J = 6.4 Hz, 2 H), 2.15-2.30 (m, 2 H), 1.75-1.88 (m, 2 H), 1.45 (s, 9 H), 1.35-1.54 (m, 1 H), 1.00-1.30 (m, 4 H).

Step C: Synthesis of *trans*-4-bromo-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-trifluoromethoxy-benzenesulfonamide.

To a suspension of *trans*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-carbamic acid *tert*-butyl ester (500 mg, 1.25 mmol) in EtOAc (5 mL) was added 4 M hydrogen chloride in EtOAc (5 mL). The mixture was stirred at ambient temperature for 1 hr and concentrated to give a white solid. To a suspension of the above solid in CH_2Cl_2 (7 mL) was added diisopropylethylamine (905 μL, 5.20 mmol). The mixture was cooled to 4 °C and a solution of 4-bromo-2-trifluoromethoxy-benzenesulfonyl chloride (446 mg, 1.31 mmol) in CH_2Cl_2 (2 mL) was added below 5 °C. The reaction mixture was stirred at 4 °C for 1.5 hr. To the reaction mixture was added a solution of 4-bromo-2-trifluoromethoxy-benzenesulfonyl chloride (85mg, 0.25 mmol) in CH_2Cl_2 (0.5 mL) and the mixture was stirred at 4 °C for 1 hr. To the reaction mixture was added diisopropylethylamine (220 μL, 1.26 mmol) and the mixture was stirred at 4 °C for 1 hr. The reaction was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica gel, 50% EtOAc in hexane) to give *trans*-4-bromo-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-trifluoromethoxy-benzenesulfonamide (624 mg, 83%) as a pale yellow solid.

ESI MS m/e 602, M + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, J = 8.9 Hz, 1 H), 7.80 (d, J = 8.5 Hz, 1 H), 7.39-7.60 (m, 4 H), 7.04 (ddd, J = 8.2, 6.8, 1.6 Hz, 1 H), 3.71-3.92 (m, 1 H), 3.30 (s, 6 H), 2.85 (d, J = 6.5 Hz, 2 H), 2.10-2.22 (m, 2 H), 1.70-1.86 (m, 2 H), 1.37-1.53 (m, 1 H), 0.98-1.32 (m, 4 H).

Example 7



***N*²-[1-(4-Bromo-2-trifluoromethoxy-benzenesulfonyl)-piperidin-4-ylmethyl]-*N*⁴,*N*⁴-dimethyl-quinazoline-2,4-diamine**

Step A: Synthesis of 4-aminomethyl-piperidine-1-carboxylic acid *tert*-butyl ester.

To a solution of *C*-piperidin-4-yl-methylamine (15.0 g, 131 mmol) in toluene (165 mL) was added benzaldehyde (13.9 g, 131 mmol) and the mixture was stirred at reflux with a Dean-Stark trap under N_2 atmosphere for 3 hr, and cooled on an ice-bath. To the reaction mixture was added $(Boc)_2O$ (31.5 g, 144 mmol) dropwise over 15 min. The mixture was stirred at ambient temperature for 2.5 days, and concentrated. To the residue was added 1 M aqueous $KHSO_4$ and the mixture was stirred at ambient temperature for 7 hr, the aqueous layer was washed with Et_2O (twice), alkalized with sodium hydroxide, and extracted with $CHCl_3$ (five times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated. The precipitate was suspended in hexane (10 mL) and the suspension was stirred at ambient temperature for 10 min. The solid was collected by filtration and dried under reduced pressure to give 4-aminomethyl-piperidine-1-carboxylic acid *tert*-butyl ester (25.8 g, 92%) as a white solid.

ESI MS m/e 215, M + H^+; ^1H NMR (300 MHz, $CDCl_3$) δ 3.85-4.22 (m, 2 H), 2.90 (d, J = 6.8 Hz, 2 H), 2.50-2.80 (m, 2 H), 1.70-2.02 (m, 3 H), 1.45 (s, 9 H), 1.10-1.28 (m, 2 H).

Step B: Synthesis of 4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-piperidine-1-carboxylic acid *tert*-butyl ester.

Using the procedure for the step G of example 1, the title compound was obtained.

ESI MS m/e 386, M + H^+; ^1H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 8.4 Hz, 1 H), 7.41-7.53 (m, 2 H), 6.99-7.06 (m, 1 H), 5.16 (brs, 1 H), 4.00-4.20 (m, 2 H), 3.41 (t, J = 6.1 Hz, 2 H), 3.26 (s, 6 H), 2.60-2.77 (m, 2 H), 1.67-1.84 (m, 3 H), 1.45 (s, 9 H), 1.11-1.28 (m, 2 H).

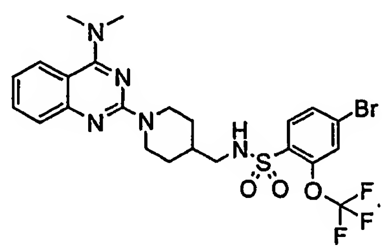
Step C: Synthesis of N^2-[1-(4-bromo-2-trifluoromethoxy-benzenesulfonyl)-piperidin-4-ylmethyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine.

To a suspension of 4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-piperidine-1-carboxylic acid *tert*-butyl ester (500 mg, 1.30 mmol) in EtOAc (5 mL) was added 4 M hydrogen chloride in EtOAc (5 mL). The mixture was stirred at ambient temperature for 1 hr and concentrated to give a white solid. To a suspension of the above solid in CH_2Cl_2 (5 mL) was added diisopropylethylamine (480 μL, 2.76 mmol). The mixture was cooled to 4 °C and a solution of 4-bromo-2-trifluoromethoxy-benzenesulfonyl chloride (462 mg, 1.36 mmol) in CH_2Cl_2 (2 mL) was added below 5 °C. The reaction

mixture was stirred at 4 °C for 3 hr. The reaction was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica gel, 14% to 20% EtOAc in hexane) to give *N*^{2}-[1-(4-bromo-2-trifluoromethoxy-benzenesulfonyl)-piperidin-4-ylmethyl]-*N*^{4},*N*^{4}-dimethyl-quinazoline-2,4-diamine (420 mg, 55%) as a yellow solid.

ESI MS m/e 588, M + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.9 Hz, 1 H), 7.81 (dd, *J* = 8.7, 0.9 Hz, 1 H), 7.40-7.56 (m, 4 H), 7.04 (ddd, *J* = 8.2, 6.7, 1.6 Hz, 1 H), 5.10-5.46 (brs, 1 H), 3.85 (d, *J* = 12.4 Hz, 2 H), 3.40 (t, *J* = 6.4 Hz, 2 H), 3.27 (s, 6 H), 2.56-2.67 (m, 2 H), 1.64-1.91 (m, 3 H), 1.23-1.43 (m, 2 H).

Example 8



4-Bromo-*N*-[1-(4-dimethylamino-quinazolin-2-yl)-piperidin-4-ylmethyl]-2-trifluoromethoxy-benzenesulfonamide

Step A: Synthesis of 4-(benzyloxycarbonylamino-methyl)-piperidine-1-carboxylic acid *tert*-butyl ester.

To a solution of 4-aminomethyl-piperidine-1-carboxylic acid tert-butyl ester (7.00 g, 32.7 mmol) in $CHCl_3$ (70 mL) was added triethylamine (3.64 g, 36.0 mmol). The resulting solution was cooled to 4 °C and ZCl (6.13 g, 35.9 mmol) was added below 8 °C over 15 min. The reaction mixture was stirred at ambient temperature for 18 hr, and poured into saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times), dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (silica gel, 33% to 50% EtOAc in hexane) to give 4-(benzyloxycarbonylamino-methyl)-piperidine-1-carboxylic acid *tert*-butyl ester (10.7 g, 94%) as a colorless oil.

ESI MS m/e 371, M + Na^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26-7.37 (m, 5 H), 5.09 (s, 2 H), 4.84-5.01 (m, 1 H), 3.95-4.22 (m, 2 H), 2.98-3.16 (m, 2 H), 2.66 (t, *J* = 12.4 Hz, 2 H),

1.58-1.72 (m, 3 H), 1.45 (s, 9 H), 0.98-1.18 (m, 2 H).

Step B: Synthesis of piperidin-4-ylmethyl-carbamic acid benzyl ester hydrochloride.

A solution of 4-(benzyloxycarbonylamino-methyl)-piperidine-1-carboxylic acid *tert*-butyl ester (10.2 g, 29.3 mmol) in EtOAc (100 mL) was cooled on an ice-bath and 4 M hydrogen chloride in EtOAc (100 mL) was added. The mixture was stirred at ambient temperature for 1 hr and concentrated. The residue was suspended in hexane (30 mL) and the mixture was stirred at ambient temperature for 30 min. The solid was collected by filtration, washed with hexane, and dried under reduced pressure to give piperidin-4-ylmethyl-carbamic acid benzyl ester hydrochloride (7.24 g, 87%) as a white solid.

ESI MS m/e 271, M (free) + Na^+; ^1H NMR (300 MHz, DMSO-d_6) δ 9.10 (brs, 2 H), 7.20-7.50 (m, 6 H), 5.02 (s, 2 H), 3.15-3.28 (m, 2 H), 2.68-3.02 (m, 4 H), 1.56-1.82 (m, 3 H), 1.20-1.52 (m, 2 H).

Step C: Synthesis of [1-(4-dimethylamino-quinazolin-2-yl)-piperidin-4-ylmethyl]-carbamic acid benzyl ester.

Using the procedure for the step C of example 3, the title compound was obtained.

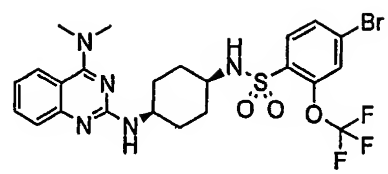
ESI MS m/e 420, M + H^+; ^1H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, J = 8.2 Hz, 1 H), 7.21-7.49 (m, 7 H), 6.95-7.04 (m, 1 H), 5.06-5.17 (m, 2 H), 4.83-4.98 (m, 3 H), 3.24 (s, 6 H), 3.00-3.16 (m, 2 H), 2.77-2.91 (m, 2 H), 1.58-1.97 (m, 3 H), 1.12-1.33 (m, 2 H).

Step D: Synthesis of 4-bromo-*N*-[1-(4-dimethylamino-quinazolin-2-yl)-piperidin-4-ylmethyl]-2-trifluoromethoxy-benzenesulfonamide.

Using the procedure for the step D of example 3, the title compound was obtained.

ESI MS m/e 588, M + H^+; ^1H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, J = 8.7 Hz, 1 H), 7.78 (d, J = 8.2 Hz, 1 H), 7.44-7.59 (m, 4 H), 6.97-7.06 (m, 1 H), 4.94-5.04 (m, 1 H), 4.89 (d, J = 13.2 Hz, 2 H), 3.25 (s, 6 H), 2.75-2.88 (m, 4 H), 1.64-1.82 (m, 3 H), 1.05-1.28 (m, 2 H).

Example 9



cis-4-Bromo-N-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-2-trifluoromethoxy-benzenesulfonamide

Step A: Synthesis of *cis*-(4-benzyloxycarbonylamino-cyclohexyl)-carbamic acid benzyl ester.

To a suspension of *cis*-cyclohexane-1,4-dicarboxylic acid (25.0 g, 145 mmol) in benzene (125 mL) were added phosphorazidic acid diphenyl ester (81.9 g, 298 mmol) and triethylamine (30.1 g, 297 mmol). The reaction mixture was stirred at reflux for 2.5 hr **(Caution! Vigorous exothermic reaction)**. Benzyl alcohol (32.2 g, 298 mmol) was added and the mixture was stirred at reflux for 24 hr. The reaction mixture was concentrated and the residue was dissolved in EtOAc and H_2O. The organic layer was separated and the aqueous layer was extracted with EtOAc (twice). The combined organic layer was washed with 1 M aqueous $KHSO_4$, saturated aqueous $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (silica gel, 33% EtOAc in hexane) to give *cis*-(4-benzyloxycarbonylamino-cyclohexyl)-carbamic acid benzyl ester (52.0 g, 94%) as a colorless oil.

ESI MS m/e 405, M + Na^+; ^1H NMR (300 MHz, $CDCl_3$) δ 7.15-7.40 (m, 10 H), 5.07 (s, 4 H), 4.70-5.00 (m, 2 H), 3.52-3.80 (m, 2 H), 1.60-1.80 (m, 4 H), 1.45-1.60 (m, 4 H).

Step B: Synthesis of *cis*-(4-amino-cyclohexyl)-carbamic acid *tert*-butyl ester.

To a solution of *cis*-(4-benzyloxycarbonylamino-cyclohexyl)-carbamic acid benzyl ester (91.7 g, 240 mmol) in MeOH (460 mL) was added 5% Pd/C (9.17 g). The reaction mixture was stirred at ambient temperature under hydrogen atmosphere for 2.5 days, filtered through a pad of celite, and concentrated to give a diamine as a colorless oil. To a solution of the diamine in MeOH (550 mL) was added a solution of $(Boc)_2O$ (6.59 g, 30.2 mmol) in MeOH (80 mL) dropwise over 4 hr. The reaction mixture was stirred at

ambient temperature for 1.5 days and concentrated. After dissolution with H_2O, the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated to give *cis*-(4-amino-cyclohexyl)-carbamic acid *tert*-butyl ester (7.78 g, 15%, crude) as a colorless oil. The aqueous layer was concentrated and the residue was dissolved in MeOH, dried over $MgSO_4$, filtered, and concentrated to give a recovered diamine (32.9 g) as a colorless oil. To a solution of the recovered diamine (32.9 g, 288 mmol) in MeOH (660 mL) was added a solution of $(Boc)_2O$ (6.29 g, 28.8 mmol) in MeOH (80 mL) dropwise over 5 hr. The reaction mixture was stirred at ambient temperature for 10 hr and concentrated. After dissolution with H_2O, the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated to give *cis*-(4-amino-cyclohexyl)-carbamic acid *tert*-butyl ester (8.16 g, 16%, crude) as a colorless oil. The aqueous layer was concentrated and the residue was dissolved in MeOH, dried over $MgSO_4$, filtered, and concentrated to give a recovered diamine (23.1 g) as a colorless oil. To a solution of the recovered diamine (23.1 g, 202 mmol) in MeOH (462 mL) was added a solution of $(Boc)_2O$ (4.42 g, 20.3 mmol) in MeOH (56 mL) dropwise over 4 hr. The reaction mixture was stirred at ambient temperature for 3.5 days and concentrated. After dissolution with H_2O, the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated to give *cis*-(4-amino-cyclohexyl)-carbamic acid *tert*-butyl ester (5.01 g, 10% based on starting material) as a colorless oil. The aqueous layer was concentrated and the residue was dissolved in MeOH, dried over $MgSO_4$, filtered, and concentrated to give a recovered diamine (16.0 g) as a colorless oil. To a solution of the recovered diamine (16.0 g, 140 mmol) in MeOH (320 mL) was added a solution of $(Boc)_2O$ (3.06 g, 14.0 mmol) in MeOH (40 mL) dropwise over 4 hr. The reaction mixture was stirred at ambient temperature for 13 hr and concentrated. After dissolution with H_2O, the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated to give *cis*-(4-amino-cyclohexyl)-carbamic acid *tert*-butyl ester (3.53 g, 7% based on the starting material) as a colorless oil. The aqueous layer was concentrated and the residue was dissolved in MeOH, dried over $MgSO_4$, filtered, and concentrated to give a recovered diamine (11.1 g) as a colorless oil.

ESI MS m/e 215, $M + H^+$; ^1H NMR (300 MHz, $CDCl_3$) δ 4.30-4.82 (m, 1 H), 3.50-3.80 (m, 1 H), 2.78-2.95 (m, 1 H), 1.44 (s, 9H), 1.20-1.80 (m, 8 H).

Step C: Synthesis of *cis*-N^2-(4-amino-cyclohexyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine.

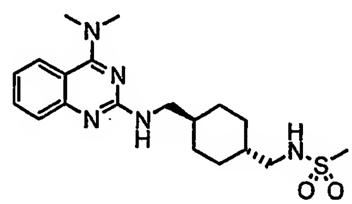
A mixture of (2-chloro-quinazolin-4-yl)-dimethyl-amine obtained in step B of example 1 (3.00 g, 14.4 mmol) and *cis*-(4-amino-cyclohexyl)-carbamic acid *tert*-butyl ester (3.72 g, 17.4 mmol) in 2-propanol (10 mL) was stirred at reflux for 5.5 days, poured into saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica, 20% EtOAc in hexane) to give *cis*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-carbamic acid *tert*-butyl ester including solvent (5.44 g) as a colorless oil. To a solution of the above material (5.44 g) in EtOAc (10 mL) was added 4 M hydrogen chloride in EtOAc (50 mL). The reaction mixture was stirred at ambient temperature for 2 hr, and concentrated. The residue was alkalized with saturated aqueous $NaHCO_3$, and the precipitate was collected by filtration to give *cis*-N^2-(4-amino-cyclohexyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine (2.26 g, 55%) as a white solid. The aqueous layer was extracted $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated to give *cis*-N^2-(4-amino-cyclohexyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine (687 mg, 17%) as a white solid.
ESI MS m/e 285, M^+; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.86 (d, J = 7.5 Hz, 1 H), 7.47 (t, J = 8.3 Hz, 1 H), 7.29 (d, J = 8.3 Hz, 1 H), 7.01 (t, J = 7.6 Hz, 1 H), 6.56 (d, J = 7.5 Hz, 1 H), 3.83-4.06 (m, 1 H), 3.38-3.52 (m, 1 H), 3.20 (s, 6 H), 1.22-1.82 (m, 8 H).

Step D: Synthesis of *cis*-4-bromo-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-2-trifluoromethoxy-benzenesulfonamide.

To a suspension of *cis*-N^2-(4-amino-cyclohexyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine (680 mg, 2.38 mmol) in CH_2Cl_2 (7 mL) was added diisopropylethylamine (620 μL, 3.56 mmol). The mixture was cooled on an ice-bath and a solution of 4-bromo-2-trifluoromethoxy-benzenesulfonyl chloride (849 mg, 2.50 mmol) in CH_2Cl_2 (3 mL) was added dropwise. The reaction mixture was stirred on an ice-bath for 6.5 hr. The reaction was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica gel, 33% EtOAc in hexane) to give *cis*-4-bromo-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-2-

trifluoromethoxy-benzenesulfonamide (782 mg, 56%) as a pale yellow solid.
ESI MS m/e 588, M^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (d, J = 8.9 Hz, 1 H), 7.81 (dd, J = 8.3, 1.2 Hz, 1 H), 7.41-7.58 (m, 4 H), 7.04 (ddd, J = 8.3, 6.6, 1.6 Hz, 1 H), 4.00-4.12 (m, 1 H), 3.36-3.45 (m, 1 H), 3.31 (s, 6 H), 1.54-1.84 (m, 8 H).

Example 10

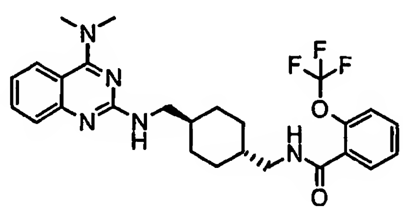


***trans*-*N*-{4-[(4-Dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-methanesulfonamide**

Step A: Synthesis of *trans*-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}- methane sulfonamide.

Using the procedure for the step H of example 1, the title compound was obtained. ESI MS m/e 392, M + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 7.8 Hz, 1 H), 7.38-7.53 (m, 2 H), 7.02 (ddd, J = 8.3, 6.6, 1.6 Hz, 1 H), 5.07 (brs, 1 H), 4.61 (brs, 1 H), 3.36 (t, J = 6.2 Hz, 2 H), 3.27 (s, 6 H), 2.94 (s, 3 H), 2.91-3.01 (m, 2 H), 1.76-1.98 (m, 4 H), 1.37-1.64 (m, 2 H), 0.85-1.12 (m, 4 H).

Example 11



***trans*-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-2-trifluoromethoxy-benzamide**

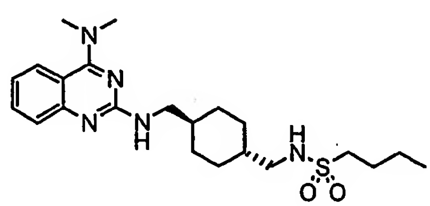
Step A: Synthesis of *trans*-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-

cyclohexylmethyl}-2-trifluoromethoxy-benzamide.

To a suspension of *trans*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]cyclohexylmethyl}-carbamic acid *tert*-butyl ester obtained in step G of example 1 (800 mg, 1.93 mmol) in EtOAc (10 mL) was added 4 M hydrogen chloride in EtOAc (10 mL). The mixture was stirred at ambient temperature for 60 min and concentrated to give a white solid. To a suspension of the solid in CH_2Cl_2 (10 mL) was added diisopropylethylamine (706 µL, 4.05 mmol). The mixture was cooled at 4 °C and a solution of 2-(trifluoromethoxy)benzoyl chloride (455 mg, 2.03 mmol) in CH_2Cl_2 (4 mL) was added below 5 °C. The reaction mixture was stirred at 4 °C for 90 min. The reaction was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica gel, 33% EtOAc in hexane) to give *trans*-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-2-trifluoromethoxy-benzamide (772 mg, 80%) as a pale yellow solid.

ESI MS m/e 502, M + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 7.4, 1.6, Hz, 1 H), 7.81 (d, *J* = 8.1 Hz, 1 H), 7.33-7.55 (m, 4 H), 7.29 (d, *J* = 8.8, Hz, 1 H), 6.96-7.08 (m, 1 H), 6.55 (brs, 1 H), 4.97 (brs, 1 H), 3.28-3.43 (m, 4 H), 3.26 (s, 6 H), 1.76-2.10 (m, 4 H), 1.44-1.72 (m, 2 H), 0.90-1.21 (m, 4 H).

Example 12



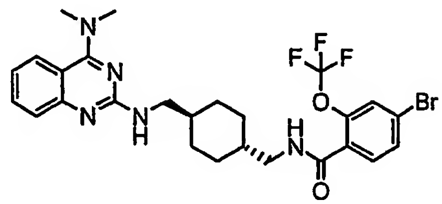
***trans*-Butane-1-sulfonic acid {4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-amide**

Step A: Synthesis of *trans*-butane-1-sulfonic acid {4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-amide.

Using the procedure for the step H of example 1, the title compound was obtained. ESI MS m/e 434, M + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.2 Hz, 1 H), 7.35-

7.54 (m, 2 H), 6.97-7.07 (m, 1 H), 4.41 (t, J = 6.1 Hz, 1 H), 3.36 (t, J = 6.1 Hz, 2 H), 3.27 (s, 6 H), 2.89-3.05 (m, 4 H), 1.71-1.97 (m,, 6 H), 1.37-1.65 (m, 4 H), 0.82-1.12 (m, 7 H).

Example 13



***trans*-4-Bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-2-trifluoromethoxy-benzamide**

Step A: Synthesis of 4-bromo-2-trifluoromethoxy-benzaldehyde.

A solution of 4-bromo-1-iodo-2-trifluoromethoxy-benzene (1.00 g, 2.72 mmol) in THF (15 mL) was cooled to –78 °C, and 2.66 M BuLi in hexane (2.05 mL, 5.44 mmol) was added dropwise. The reaction mixture was stirred at –78 °C for 1.5 h, and *N*-formylmorpholine (0.57 mL, 5.63 mmol) was added. The reaction mixture was stirred at –78 °C for 15 min and at ambient temperature for 80 min. The reaction was quenched with 0.25 M aqueous citric acid (10 mL), and the resulting mixture was extracted with EtOAc (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (silica gel, 2% to 5% EtOAc in hexane) to give 4-bromo-2-trifluoromethoxy-benzaldehyde (560 mg, 77%) as a pale brown solid.

CI MS m/e 269, M + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.33 (s, 1 H), 7.85 (d, J = 8.1 Hz, 1 H), 7.50-7.67 (m, 2 H).

Srep B: Synthesis of 4-bromo-2-trifluoromethoxy-benzoic acid.

A solution of 4-bromo-2-trifluoromethoxy-benzaldehyde (550 mg, 2.04 mmol) in 1,4-dioxane (27 mL) and H_2O (9 mL) was cooled at 4 °C. To the solution were added amidosulfuric acid (296 mg, 3.05 mmol) and sodium dihydrogen phosphate dihydrate (1.4 g, 8.98 mmol). The mixture was stirred at 4 °C for 15 min. To the reaction mixture was added a solution of sodium chlorite (238 mg, 2.63 mmol) in H_2O (1.5 mL) and stirred at 4 °C for 15 min. To the reaction mixture was added Na_2CO_3 (304 mg, 2.41 mmol) and stirred

at 4 °C for 15 min. The mixture was acidified with conc-HCl (pH = 1), and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (silica gel, 1% MeOH in $CHCl_3$) to give 4-bromo-2-trifluoromethoxy-benzoic acid (471 mg, 81%) as a white solid.

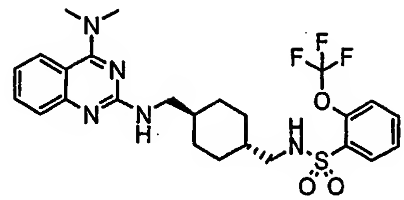
ESI MS m/e 284, M^+; ^1H NMR (300 MHz, $CDCl_3$) δ 7.98 (d, J = 8.4 Hz, 1 H), 7.53-7.62 (m, 2 H).

Step C: Synthesis of *trans*-4-bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-2-trifluoromethoxy-benzamide.

To a solution of 4-bromo-2-trifluoromethoxy-benzoic acid (454 mg, 1.59 mmol) in CH_2Cl_2 (6 mL) were added DMF (1.5 μL, 0.02 mmol) and $SOCl_2$ (158 μL, 2.17 mmol). The mixture was stirred at reflux for 1 hr and concentrated to give acid chloride as a pale yellow oil. To a suspension of *trans*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]cyclohexylmethyl}-carbamic acid *tert*-butyl ester obtained in step G of example 1 (624 mg, 1.51 mmol) in EtOAc (10 mL) was added 4 M hydrogen chloride in EtOAc (8 mL). The mixture was stirred at ambient temperature for 40 min and concentrated to give a white solid. To a suspension of the solid in CH_2Cl_2 (6 mL) was added diisopropylethylamine (552 μL, 3.17 mmol). The mixture was cooled at 4 °C and a solution of acid chloride in CH_2Cl_2 (6 mL) was added below 5 °C. The reaction mixture was stirred at 4 °C for 2.5 hr. The reaction was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica gel, 33% EtOAc in hexane) to give *trans*-4-bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-2-trifluoromethoxy-benzamide (309 mg, 35%) as a pale yellow solid.

ESI MS m/e 580, M + H^+; ^1H NMR (300 MHz, $CDCl_3$) δ 7.89 (d, J = 8.4 Hz, 1 H), 7.81 (d, J = 8.2 Hz, 1 H), 7.39-7.67 (m, 4 H), 7.02 (ddd, J = 8.2, 6.4, 1.9 Hz, 1 H), 6.53 (brs, 1 H), 4.99 (brs, 1 H), 3.37 (t, J = 6.5 Hz, 2 H), 3.32 (t, J = 6.3 Hz, 2 H), 3.27 (s, 6 H), 1.76-2.02 (m,, 4 H), 1.48-1.67 (m, 2 H), 0.94-1.16 (m, 4 H).

Example 14



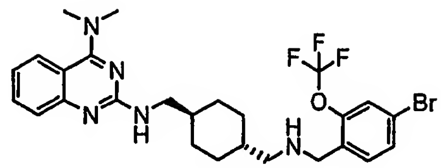
***trans-N*-{4-[(4-Dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-2-trifluoromethoxy-benzenesulfonamide.**

Step A: Synthesis of *trans-N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-2-trifluoromethoxy-benzenesulfonamide.

To a suspension of *trans*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]cyclohexylmethyl}-carbamic acid *tert*-butyl ester obtained in step G of example 1 (500 mg, 1.21 mmol) in EtOAc (8 mL) was added 4 M hydrogen chloride in EtOAc (7 mL). The mixture was stirred at ambient temperature for 40 min and concentrated to give a white solid. To a suspension of the solid in CH_2Cl_2 (7 mL) was added pyridine (215 μL, 2.66 mmol). The mixture was cooled at 4 °C and a solution of 2-trifluoromethoxy-benzenesulfonyl chloride (331 mg, 1.27 mmol) in CH_2Cl_2 (2 mL) was added below 5 °C. The reaction mixture was stirred at 4 °C for 2 hr. The reaction was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica gel, 20% EtOAc in hexane) to give *trans-N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-2-trifluoromethoxy-benzenesulfonamide (231 mg, 36%) as a pale yellow solid.

ESI MS m/e 538, M + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (dd, J = 8.0, 1.6 Hz, 1 H), 7.81 (d, J = 8.2 Hz, 1 H), 7.57-7.66 (m, 1 H), 7.36-7.52 (m, 4 H), 7.02 (ddd, J = 8.3, 6.5, 1.7 Hz, 1 H), 4.94 (brs, 1 H), 4.66 (brs, 1 H), 3.34 (t, J = 6.4 Hz, 2 H), 3.26 (s, 6 H), 2.78 (t, J = 6.2 Hz, 2 H), 1.68-2.01 (m, 4 H), 1.29-1.60 (m, 2 H), 0.79-1.07 (m, 4 H).

Example 15



***trans*-N^2-{4-[(4-Bromo-2-trifluoromethoxy-benzylamino)-methyl]-cyclohexylmethyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine**

Step A: Synthesis of *trans*-N^2-(4-aminomethyl-cyclohexylmethyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine.

To a suspension of *trans*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-carbamic acid *tert*-butyl ester (20.1 g, 48.6 mmol) in EtOAc (200 mL) was added 4 M hydrogen chloride in EtOAc (200 mL). The mixture was stirred at ambient temperature for 90 min and concentrated to give a solid. The solid was alkalized with saturated aqueous $NaHCO_3$ (pH = 9), concentrated, and purified by flash chromatography (NH silica gel, 33% MeOH in $CHCl_3$) to give *trans*-N^2-(4-aminomethyl-cyclohexylmethyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine (14.7 g, 97%) as a white solid. ESI MS m/e 314, M + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 8.2 Hz, 1 H), 7.42-7.52 (m, 2 H), 7.01 (ddd, J = 8.2, 6.2, 0.9 Hz, 1 H), 4.95 (brs, 1 H), 3.36 (t, J = 6.3 Hz, 2 H), 3.26 (s, 6 H), 2.52 (d, J = 6.4 Hz, 2 H), 1.75-1.96 (m, 5 H), 1.48-1.66 (m, 1 H), 0.82-1.40 (m, 6 H).

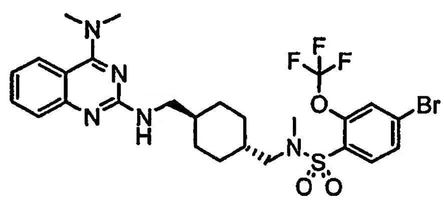
Step B: Synthesis of *trans*-N^2-{4-[(4-bromo-2-trifluoromethoxy-benzylamino)-methyl]-cyclohexylmethyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine.

To a solution of *trans*-N^2-(4-aminomethyl-cyclohexylmethyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine (500 mg, 1.59 mmol) in CH_2Cl_2 (5 mL) were added 4-bromo-2-trifluoromethoxy-benzaldehyde obtained in step A of example 13 (428 mg, 1.59 mmol), acetic acid (95 mg, 1.59 mmol), and $NaBH(OAc)_3$ (505 mg, 2.38 mmol). The reaction mixture was stirred at ambient temperature for 4 hr. The reaction was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by

flash chromatography (NH-silica gel, 50% EtOAc in hexane) to give *trans*-N^2-{4-[(4-bromo-2-trifluoromethoxy-benzylamino)-methyl]-cyclohexylmethyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine (783 mg, 89%) as a pale yellow solid.

ESI MS m/e 566, M + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.2 Hz, 1 H), 7.34-7.52 (m, 5 H), 7.01 (ddd, *J* = 8.3, 6.2, 2.0 Hz, 1 H), 5.00 (brs, 1 H), 3.77 (s, 2 H), 3.36 (t, *J* = 6.3 Hz, 2 H), 3.26 (s, 6 H), 2.43 (d, *J* = 6.7 Hz, 2 H), 1.76-1.95 (m,, 4 H), 1.34-1.65 (m, 2 H), 0.83-1.12 (m, 4 H).

Example 16



***trans*-4-Bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-*N*-methyl-2-trifluoromethoxy-benzenesulfonamide**

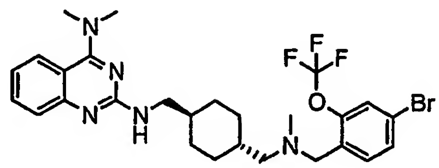
Step A: Synthesis of *trans*-4-bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-*N*-methyl-2-trifluoromethoxy-benzenesulfonamide.

To a solution of *trans*-4-bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-2-trifluoromethoxy-benzenesulfonamide obtained in step H of example 1 (380 mg, 0.61 mmol) in DMF (2 mL) was added 60% sodium hydride in oil (24.6 mg, 0.61 mmol). The reaction mixture was stirred at ambient temperature for 80 min. The reaction mixture was cooled at 0 °C and iodomethane (38.3 μL, 0.61 mmol) was added and stirred at ambient temperature for 3 hr. The reaction was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with EtOAc (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica gel, 25% EtOAc in hexane, and silica gel, 5% MeOH in $CHCl_3$) to give *trans*-4-bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-*N*-methyl-2-trifluoromethoxy-benzenesulfonamide (268 mg, 69%) as a pale yellow solid.

ESI MS m/e 630, M + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, *J* = 9.2 Hz, 1 H), 7.81 (d,

J = 8.4 Hz, 1 H), 7.41-7.57 (m, 4 H), 7.03 (ddd, J = 8.4, 6.3, 1.8 Hz, 1 H), 3.37 (t, J = 6.2 Hz, 2 H), 3.27 (s, 6 H), 2.97 (d, J = 7.5 Hz, 2H), 2.81 (s, 3H), 1.73-1.97 (m, 4H), 1.46-1.66 (m, 2H), 0.83-1.12 (m, 4H).

Example 17



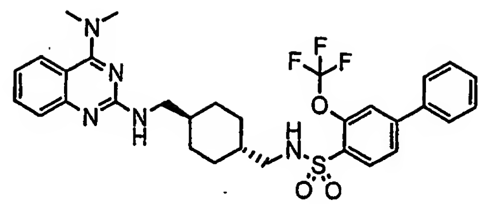
***trans*-N^2-(4-{[(4-Bromo-2-trifluoromethoxy-benzyl)-methyl-amino] -methyl}-cyclohexylmethyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine**

Step A: Synthesis of *trans*-N^2-(4-{[(4-bromo-2-trifluoromethoxy-benzyl)-methyl-amino]-methyl}-cyclohexylmethyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine.

To a solution of *trans*- N^2-{4-[(4-bromo-2-trifluoromethoxy-benzylamino)-methyl] -cyclohexylmethyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine obtained in step B of example 15 (290 mg, 0.52 mmol) in CH_2Cl_2 (3 mL) were added 37% aqueous formaldehyde (42 mg, 0.52 mmol), acetic acid (31 mg, 0.52 mmol), and $NaBH(OAc)_3$ (165 mg, 0.78 mmol). The reaction mixture was stirred at ambient temperature for 19 hr. The reaction was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica gel, 25% EtOAc in hexane) to give *trans*-N^2-(4-{[(4-bromo-2-trifluoromethoxy-benzyl)-methyl-amino]-methyl}-cyclohexylmethyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine (153 mg, 51%) as a pale yellow solid.

ESI MS m/e 580, M + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 7.6 Hz, 1 H), 7.34-7.53 (m, 5 H), 7.02 (ddd, J = 8.3, 6.2, 2.0 Hz, 1 H), 3.44 (s, 2 H), 3.36 (t, J = 6.3 Hz, 2 H), 3.27 (s, 6 H), 2.14 (s, 3H), 2.11-2.18 (m, 2 H), 1.81-1.96 (m,, 4H), 1.36-1.66 (m, 2 H), 0.73-1.13 (m, 4 H).

Example 18



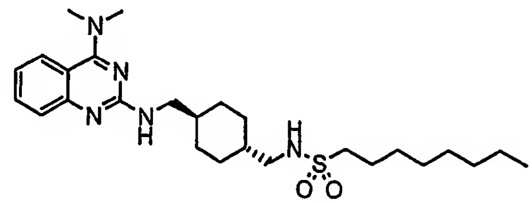
***trans*- 3-Trifluoromethoxy-biphenyl-4-sulfonic acid {4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-amide**

Step A: Synthesis of *trans*- 3-trifluoromethoxy-biphenyl-4-sulfonic acid {4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-amide.

To a solution of *trans*-4-bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-2-trifluoromethoxy-benzenesulfonamide obtained in step H of example 1 (122 mg, 0.198 mmol) in toluene (2.7 mL) were added MeOH (0.9 mL), 2 M aqueous K_2CO_3 (0.9 mL), phenylboronic acid (29.0 mg, 0.237 mmol), and tetrakis(triphenylphosphine)palladium (23.0 mg, 0.02 mmol). The reaction mixture was stirred at 130 °C for 10 hr. The mixture was poured into water, and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica gel, 25% EtOAc in hexane and silica gel, 9% MeOH in $CHCl_3$) to give *trans*-3-trifluoromethoxy-biphenyl-4-sulfonic acid {4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-amide (77 mg, 0.125 mmol) as a white solid.

ESI MS m/e 614, M + H^+; ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.07 (d, J = 8.4 Hz, 1 H), 7.82 (d, J = 8.8 Hz, 1 H), 7.38-7.67 (m, 9 H), 7.03 (ddd, J = 8.4, 6.2, 2.2 Hz, 1 H), 5.11 (brs, 1 H), 4.71 (brs, 1 H), 3.35 (t, J = 6.2 Hz, 2 H), 3.27 (s, 6 H), 2.73-2.90 (m, 2 H), 1.67-2.03 (m,, 4 H), 1.30-1.64 (m, 2 H), 0.75-1.16 (m, 4 H).

Example 19

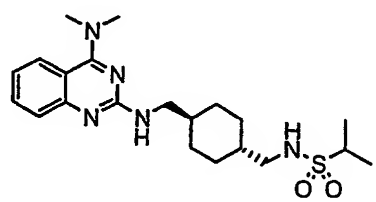


***trans*-Octane-1-sulfonic acid{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-amide**

Step A: Synthesis of *trans*-octane-1-sulfonic acid{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-amide.

Using the procedure for the step H of example 1, the title compound was obtained. ESI MS m/e 490, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 7.8 Hz, 1 H), 7.38-7.54 (m, 2 H), 7.02 (ddd, J = 8.3, 6.6, 1.7 Hz, 1 H), 5.01 (brs, 1 H), 4.45 (t, J = 6.2 Hz, 1 H), 3.36 (t, J = 6.2 Hz, 2 H), 3.26 (s, 6 H), 2.86-3.04 (m, 4 H), 1.70-1.96 (m, 6 H), 1.12-1.65 (m, 11 H), 0.76-1.11 (m, 8 H).

Example 20



***trans*-Propane-2-sulfonic acid {4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-amide**

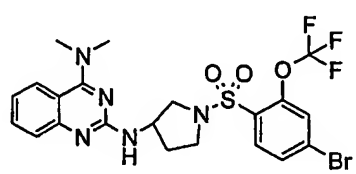
Step A: Synthesis of *trans*- propane-2-sulfonic acid {4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-amide.

To a suspension of *trans*-N^2-(4-aminomethyl-cyclohexylmethyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine obtained in step A of example 15 (227 mg, 0.72 mmol) in CH_2Cl_2 (4 mL) was added diisopropylethylamine (263 µL, 1.51 mmol). The mixture was cooled at 4 °C and a solution of 2-propanesulfonyl chloride (108 mg, 0.76 mmol) in CH_2Cl_2 (1 mL)

was added below 5 °C. The reaction mixture was stirred at ambient temperature for 12 hr. The reaction was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica gel, 66% EtOAc in hexane) to give *trans*-propane-2-sulfonic acid {4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-amide (135 mg, 45%) as a pale yellow solid.

ESI MS m/e 420, M + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 7.8 Hz, 1 H), 7.39-7.52 (m, 2 H), 7.02 (ddd, J = 8.3, 6.5, 1.7 Hz, 1 H), 5.02 (brs, 1 H), 4.22 (t, J = 6.2 Hz, 1 H), 3.36 (t, J = 6.2 Hz, 2 H), 3.27 (s, 6 H), 3.09-3.21 (m, 1 H), 2.97 (t, J = 6.5 Hz, 2 H), 1.75-1.97 (m, 4 H), 1.39-1.64 (m, 2 H), 1.37 (d, J = 6.8 Hz, 6 H), 0.85-1.12 (m, 4 H).

Example 21



***N*^{2}-[1-(4-Bromo-2-trifluoromethoxy-benzenesulfonyl)-pyrrolidin-3-yl]-*N*^{4},*N*^{4}-dimethyl-quinazoline-2,4-diamine**

Step A: Synthesis of 1-(4-bromo-2-trifluoromethoxy-benzenesulfonyl)-pyrrolidin-3-ylamine hydrochloride.

To a solution of pyrrolidin-3-yl-carbamic acid *tert*-butyl ester (1.00 g, 5.37 mmol) in CH_2Cl_2 (10 mL) was added diisopropylethylamine (1.96 mL, 5.92 mmol). The mixture was cooled at 0 °C and a solution of 4-bromo-2-trifluoromethoxy-benzenesulfonyl chloride (2.01 g, 5.92 mmol) in CH_2Cl_2 (10 mL) was added below 10 °C. The reaction mixture was stirred at 4 °C for 15 min, dissolved in $CHCl_3$ and saturated aqueous $NaHCO_3$. The two phases were separated, the aqueous layer was extracted with $CHCl_3$ (twice). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and dried under reduced pressure to give a pale brown solid. To a solution of the above solid in $CHCl_3$ (50 mL) was added 4 M hydrogen chloride in EtOAc (50 mL). The mixture was stirred at ambient temperature for 1 hr, filtered, washed with EtOAc, and dried under reduced pressure to

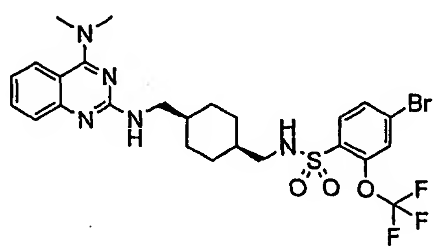
give 1-(4-bromo-2-trifluoromethoxy-benzenesulfonyl)-pyrrolidin-3-ylamine hydrochloride (1.83 g, 80%) as a white solid.

ESI MS m/e 388, M^+; ^{1}H NMR (300 MHz, DMSO-d_6) δ 8.44 (brs, 3 H), 7.82-7.94 (m, 3 H), 3.76-3.84 (m, 1 H), 3.42-3.58 (m, 2 H), 3.23-3.40 (m, 2 H), 2.10-2.23 (m, 1 H), 1.88-2.02 (m, 1 H).

Step B: Synthesis of *N*^{2}-[1-(4-bromo-2-trifluoromethoxy-benzenesulfonyl)-pyrrolidin-3-yl]-*N*^{4},*N*^{4}-dimethyl-quinazoline-2,4-diamine

Using the procedure for the step C of example 3, the title compound was obtained. ESI MS m/e 560, M + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82-7.89 (m, 2 H), 7.40-7.75 (m, 4 H), 7.08 (ddd, J = 8.3, 6.8, 1.5 Hz, 1 H), 4.83 (brs, 1 H), 4.53-4.64 (m, 1 H), 3.75 (dd, J = 10.3, 5.8 Hz, 1 H), 3.48-3.64 (m, 2 H), 3.44 (dd, J = 10.3, 4.4 Hz, 1 H), 3.27 (s, 6 H), 2.21-2.36 (m, 1 H), 1.86-2.00 (m, 1 H).

Example 22



***cis*-4-Bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-2-trifluoromethoxy-benzenesulfonamide**

Step A: Synthesis of *cis*-[4-(*tert*-butoxycarbonylamino-methyl)-cyclohexylmethyl]-carbamic acid *tert*-butyl ester.

To MeOH (220 mL) cooled at 0 °C was added thionyl chloride (52 mL) below 10 °C over 2.5 hr and the solution was stirred at 0 °C for 1 hr. To the reaction mixture was added *cis*-cyclohexane-1,4-dicarboxylic acid (30.0 g, 174 mmol) and the mixture was stirred at ambient temperature for 14 hr and concentrated. The residue was dissolved in $CHCl_3$, poured into saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated. A suspension of lithium aluminum hydride (13.2 g, 348 mmol) in THF (400 mL) was cooled at –20 °C. A solution of the above residue in THF (200 mL) was added

dropwise, and the mixture was stirred at ambient temperature for 3 hr. The reaction was quenched with $Na_2SO_4 \cdot 10H_2O$, filtered through a pad of celite, and concentrated. To a solution of the above residue in toluene (500 mL) was added triphenylphosphine (37.2 g, 142 mmol). To the mixture cooled at 4 °C were added phthalimide (20.9 g, 142 mmol) and 40% diethyl azodicarboxylate (DEAD) in toluene (61.7 mL, 136 mmol) over 25 min. The reaction mixture was stirred at ambient temperature for 12 hr, poured into H_2O. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated. The precipitate was suspended in Et_2O, filtered, washed with MeOH and Et_2O, and dried under reduced pressure to give a white solid (16.5 g). To a suspension of the above solid (16.5 g, 41.0 mmol) in EtOH (735 mL) was added hydrazine hydrate (20.5 g, 410 mmol). The mixture was stirred at reflux for 2.5 hr, cooled, and concentrated. The precipitate was dissolved in 10% aqueous sodium hydroxide (120 mL) and 1, 4-dioxane (160 mL). To the mixture cooled on an ice-bath was added $(Boc)_2O$ (30.4 g, 139 mmol) and the mixture was stirred at ambient temperature for 2.5 hr, and poured into H_2O. The aqueous layer was extracted with $CHCl_3$ (ten times). The combined organic layer was dried over $MgSO_4$, filtered and concentrated. The precipitate was suspended in hexane, filtered, washed with hexane, and dried under reduced pressure to give *cis*-[4-(*tert*-butoxycarbonylamino-methyl)-cyclohexylmethyl]-carbamic acid *tert*-butyl ester (5.10 g, 9%) as a white solid.

ESI MS m/e 365, M + Na^+; ^1H NMR (300 MHz, $CDCl_3$) δ 4.49-4.59 (m, 2 H), 3.05 (t, J = 6.6 Hz, 4 H), 1.29-1.69 (m, 28 H).

Step C: Synthesis of *cis*-(4-aminomethyl-cyclohexylmethyl)-carbamic acid *tert*-butyl ester.

To a solution of *cis*-[4-(*tert*-butoxycarbonylamino-methyl)-cyclohexylmethyl]-carbamic acid *tert*-butyl ester (2.55 g, 7.45 mmol) in CH_2Cl_2 (40 mL) was added 4 M hydrogen chloride in EtOAc (4 mL). The reaction mixture was stirred at ambient temperature for 5 hr and concentrated. The residue was dissolved in 1,4-dioxane (20 mL) and 10% aqueous sodium hydroxide (40 mL) and the resulting solution was cooled on an ice-bath. $(Boc)_2O$ (829 mg, 3.80 mmol) was added dropwise and the mixture was stirred at ambient temperature for 3 h. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered and concentrated, and purified by flash chromatography (silica gel, 9% MeOH in $CHCl_3$) to give *cis*-(4-aminomethyl-

cyclohexylmethyl)-carbamic acid *tert*-butyl ester (255 mg, 14%) as a pale yellow oil. ESI MS m/e 243, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.58 (brs, 1 H), 3.06 (t, J = 6.7 Hz, 2 H), 2.60 (d, J = 5.9 Hz, 2 H), 1.28-1.70 (m, 19 H).

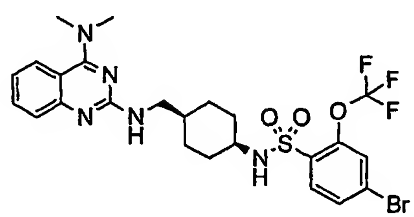
Step D: Synthesis of *cis*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-carbamic acid *tert*-butyl ester.

Using the procedure for the step G of example 1, the title compound was obtained. ESI MS m/e 414, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 7.8 Hz, 1 H), 7.42-7.52 (m, 2 H), 7.02 (ddd, J = 8.3, 6.3, 1.9 Hz, 1 H), 4.52 (brs, 1 H), 3.45 (t, J = 6.6 Hz, 2 H), 3.27 (s, 6 H), 3.08 (t, J = 6.5 Hz, 2 H), 1.34-1.86 (m, 19 H).

Step E: Synthesis of *cis*-4-bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-2-trifluoromethoxy-benzenesulfonamide.

Using the procedure for the step H of example 1, the title compound was obtained. ESI MS m/e 616, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, J = 8.9 Hz, 1 H), 7.81 (d, J = 7.8 Hz, 1 H), 7.41-7.58 (m, 4 H), 7.03 (ddd, J = 8.2, 6.6, 1.5 Hz, 1 H), 3.41 (t, J = 6.5 Hz, 2 H), 3.50 (s, 6 H), 2.90 (d, J = 7.3 Hz, 2 H), 1.32-1.86 (m, 10 H).

Example 23



***cis*-4-Bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexyl}-2-trifluoromethoxy-benzenesulfonamide**

Step A: Synthesis of *cis*-(4-hydroxymethyl-cyclohexyl)-carbamic acid *tert*-butyl ester..

A suspension of *cis*-4-amino-cyclohexanecarboxylic acid (244 g, 1.70 mol) in MeOH (2.45 L) was cooled to –8 °C. Thionyl chloride (45.0 mL, 617 mmol) was added dropwise. The resulting solution was stirred at ambient temperature for 4.5 hr and concentrated to give a white solid. To a suspension of the above solid in $CHCl_3$ (3.00 L)

were added triethylamine (261 mL, 1.87 mol) and $(Boc)_2O$ (409 g, 1.87 mol) successively. The reaction mixture was stirred at ambient temperature for 5 hr and poured into water. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (silica gel, $CHCl_3$ only to 10% MeOH in $CHCl_3$) to give a colorless oil (531 g). To a suspension cooled at –4 °C of lithium aluminum hydride (78.3 g, 2.06 mol) in Et_2O (7.9 L) was added a solution of above oil (530.9 g) in Et_2O (5.3 L) below 0 °C. The resulting suspension was stirred at ambient temperature for 2 hr. The reaction mixture was cooled on an ice-bath, quenched with cold water, filtered through a pad of celite. The filtrate was dried over $MgSO_4$, filtered, and concentrated. The precipitate was suspended in hexane (300 mL), filtered, washed with hexane, and dried under reduced pressure to give *cis*-(4-hydroxymethyl-cyclohexyl)-carbamic acid *tert*-butyl ester (301 g, 77%) as a white solid. ESI MS m/e 252, M + Na^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.30-4.82 (m, 1 H), 3.75 (brs, 1 H), 3.51 (d, J = 6.2 Hz, 1 H), 1.52-1.77 (m, 7 H), 1.45 (s, 9 H), 1.16-1.36 (m, 2 H).

Step B: Synthesis of *cis*-[4-(benzyloxycarbonylamino-methyl)-cyclohexyl]-carbamic acid *tert*-butyl ester.

To a solution of *cis*-(4-hydroxymethyl-cyclohexyl)-carbamic acid *tert*-butyl ester (17.7 g, 77.2 mmol) in THF (245 mL) were added triphenylphosphine (20.2 g, 77.0 mmol) and phthalimide (11.4 g, 77.5 mmol) successively. The resulting suspension was cooled on an ice-bath and 40% diethyl azodicarboxylate (DEAD) in toluene was added over 1 hr. The reaction mixture was stirred at ambient temperature for 2.5 days, concentrated, and purified by flash chromatography (silica gel, 33% EtOAc in hexane) to give a white solid. To a suspension of above solid (27.5 g) in EtOH (275 mL) was added hydrazine hydrate (5.76 g, 115 mmol). The mixture was stirred at reflux for 2.25 hr, cooled, concentrated. The precipitate was dissolved in 10% aqueous sodium hydroxide (350 mL). The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered and concentrated. To a solution of the above residue in $CHCl_3$ (275 mL) was added triethylamine (8.54 g, 84.4 mmol). The resulting solution was cooled to 0 °C and ZCl (14.4 g, 84.4 mmol) was added below 5 °C. The reaction mixture was stirred at ambient temperature for 16 hr, and poured into saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (silica gel, 2%

MeOH in $CHCl_3$) to give *cis*-[4-(benzyloxycarbonylamino-methyl)-cyclohexyl]-carbamic acid *tert*-butyl ester (25.3 g, 91%) as a colorless oil.

ESI MS m/e 385, M + Na^+; ^1H NMR (300 MHz, $CDCl_3$) δ 7.27-7.38 (m, 5 H), 5.09 (s, 2 H), 4.76-4.92 (m, 1 H), 4.42-4.76 (m, 1 H), 3.72 (brs, 1 H), 3.10 (t, J = 6.4 Hz, 2 H), 1.48-1.75 (m, 7 H), 1.44 (s, 9 H), 1.13-1.31 (m, 2 H).

Step C: Synthesis of *cis*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexyl}-carbamic acid *tert*-butyl ester.

A mixture of *cis*-[4-(benzyloxycarbonylamino-methyl)-cyclohexyl]-carbamic acid *tert*-butyl ester (4.00 g, 11.0 mmol) and 5% Pd/C (400 mg) in MeOH (40 mL) was stirred under hydrogen atmosphere at ambient temperature for 8.5 hr and at 50 °C for 12 hr, filtered through a pad of celite, and concentrated. The precipitate was suspended in hexane and the suspension was stirred at ambient temperature for 30 min. The solid was collected by filtration, washed with hexane, and dried (3.03 g). A mixture of (2-chloro-quinazolin-4-yl)-dimethyl-amine obtained in step B of example 1 (1.00 g, 4.82 mmol) and the above solid (1.65 g, 7.23 mmol) in 2-propanol (10 mL) was stirred at reflux for 5 days, poured into saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica gel, 20% EtOAc in hexane) to give *cis*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexyl}-carbamic acid *tert*-butyl ester (629 mg, 43%) as a pale yellow solid.

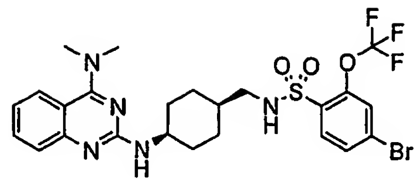
ESI MS m/e 400, M + H^+; ^1H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 8.2 Hz, 1 H), 7.42-7.56 (m, 2 H), 6.98-7.06 (m, 1 H), 4.64-4.75 (m, 1 H), 3.67-3.82 (m, 1 H), 3.29-3.44 (m, 2 H), 3.28 (s, 6 H), 1.50-1.78 (m, 7 H), 1.45 (s, 9 H), 1.21-1.42 (m, 2 H).

Step D: Synthesis of *cis*-4-bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexyl}-2-trifluoromethoxy-benzenesulfonamid.

Using the procedure for the step H of example 1, the title compound was obtained.

ESI MS m/e 602, M + H^+; ^1H NMR (300 MHz, $CDCl_3$) δ 7.91 (d, J = 8.9 Hz, 1 H), 7.82 (dd, J = 8.0, 1.0 Hz, 1 H), 7.42-7.56 (m, 4 H), 7.04 (ddd, J = 8.3, 6.6, 1.6 Hz, 1 H), 3.44-3.50 (m, 1 H), 3.40 (t, J = 6.0 Hz, 2 H), 3.28 (s, 6 H), 1.22-1.78 (m, 9 H).

Example 24



***cis*-4-Bromo-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-trifluoromethoxy-benzenesulfonamide**

Step A: Synthesis of *cis*-(4-amino-cyclohexylmethyl)-carbamic acid benzyl ester.

To a solution of *cis*-[4-(benzyloxycarbonylamino-methyl)-cyclohexyl]-carbamic acid *tert*-butyl ester obtained in step C of example 23 (12.9 g, 35.6 mmol) in EtOAc (129 mL) was added 4 M hydrogen chloride in EtOAc (129 mL). The reaction mixture was stirred at ambient temperature for 3 hr, filtered, washed with EtOAc, and dried under reduced pressure. The solid was dissolved in saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (five times), dried over $MgSO_4$, filtered and concentrated, and dried under reduced pressure to give *cis*-(4-amino-cyclohexylmethyl)-carbamic acid benzyl ester (8.88 g, 95%) as a colorless oil.

ESI MS m/e 263, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (s, 5 H), 5.12 (brs, 3 H), 2.96-3.32 (m, 3 H), 1.36-1.98 (m, 9 H).

Step B: Synthesis of *cis*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-carbamic acid benzyl ester.

Using the procedure for the step G of example 1, the title compound was obtained.

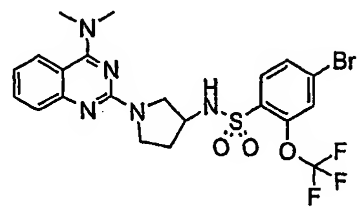
ESI MS m/e 434, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 9.0 Hz, 1 H), 7.26-7.52 (m, 7 H), 7.01 (ddd, J = 8.2, 6.5, 1.7 Hz, 1 H), 5.10 (s, 2 H), 4.93-5.06 (m, 1 H), 4.82-4.93 (m, 1 H), 4.18-4.28 (m, 1 H), 3.26 (s, 6 H), 3.11 (t, J = 6.3 Hz, 2 H), 1.80-1.93 (m, 2 H), 1.52-1.73 (m, 5 H), 1.23-1.40 (m, 2 H).

Step C: Synthesis of *cis*-4-bromo-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-trifluoromethoxy-benzenesulfonamide.

Using the procedure for the step D of example 3, the title compound was obtained.

ESI MS m/e 602, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, J = 8.9 Hz, 1 H), 7.81 (dd, J = 8.3, 1.3 Hz, 1 H), 7.38-7.59 (m, 4 H), 7.02 (ddd, J = 8.2, 6.8, 1.2 Hz, 1 H), 4.75-5.24 (m, 1 H), 4.16-4.27 (m, 1 H), 3.27 (s, 6 H), 2.86 (d, J = 6.4 Hz, 2 H), 1.78-1.91 (m, 2 H), 1.51-1.70 (m, 5 H), 1.21-1.38 (m, 2 H).

Example 25



4-Bromo-*N*-[1-(4-dimethylamino-quinazolin-2-yl)-pyrrolidin-3-yl]-2-trifluoromethoxy-benzenesulfonamide

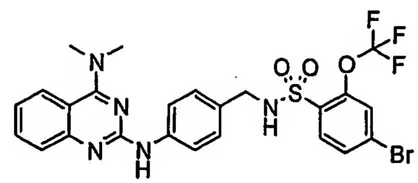
Step A: Synthesis of [1-(4-dimethylamino-quinazolin-2-yl)-pyrrolidin-3-yl]-carbamic acid *tert*-butyl ester.

Using the procedure for the step G of example 1, the title compound was obtained. ESI MS m/e 358, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 8.2 Hz, 1 H), 7.45-7.54 (m, 2 H), 6.98-7.05 (m, 1 H), 4.67-4.80 (m, 1 H), 4.25-4.40 (m, 1 H), 3.85-3.94 (m, 1 H), 3.68-3.79 (m, 2 H), 3.52-3.62 (m, 1 H), 3.27 (s, 6 H), 2.16-2.28 (m, 1 H), 1.86-2.01 (m, 1 H), 1.45 (s, 9 H).

Step B: Synthesis of 4-bromo-*N*-[1-(4-dimethylamino-quinazolin-2-yl)-pyrrolidin-3-yl]-2-trifluoromethoxy-benzenesulfonamide.

Using the procedure for the step H of example 1, the title compound was obtained. ESI MS m/e 560, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (d, J = 8.4 Hz, 1 H), 7.81 (d, J = 8.1 Hz, 1 H), 7.44-7.58 (m, 4 H), 7.03 (ddd, J = 8.4, 5.7, 2.6 Hz, 1 H), 4.76-5.04 (m, 1 H), 3.96-4.11 (m, 1 H), 3.70-3.82 (m, 2 H), 3.58-3.68 (m, 1 H), 3.45-3.54 (m, 1 H), 3.25 (s, 6 H), 2.11-2.24 (m, 1 H), 1.86-1.99 (m, 1 H).

Example 26



4-Bromo-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-benzyl]-2-trifluoromethoxy-benzene sulfonamide

Step A: Synthesis of (4-amino-benzyl)-carbamic acid *tert*-butyl ester.

To a solution of 4-aminomethyl-phenylamine (1.00 g, 8.19 mmol) in $CHCl_3$ (10 mL) was added triethylamine (870 mg, 8.60 mmol). After cooling on an ice-bath, $(Boc)_2O$ (1.88 g, 8.61 mmol) was added dropwise. The reaction mixture was stirred at ambient temperature for 55 min and poured into saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (silica gel, 9% MeOH in $CHCl_3$) to give (4-amino-benzyl)-carbamic acid *tert*-butyl ester (1.79 g, 99%) as a yellow solid.

ESI MS m/e 245, M + Na^+; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.07 (d, J = 8.4 Hz, 2 H), 6.63 (d, J = 8.4 Hz, 2 H), 4.76 (brs, 1 H), 4.18 (d, J = 5.3 Hz, 2 H), 3.65 (brs, 2 H), 1.45 (s, 9 H).

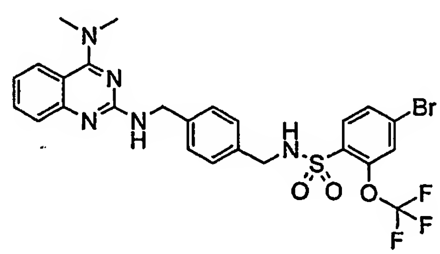
Step B: Synthesis of 4-bromo-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-benzyl]-2-trifluoromethoxy-benzenesulfonamide.

A mixture of (2-chloro-quinazolin-4-yl)-dimethyl-amine obtained in step B of example 1 (1.00 g, 4.82 mmol) and (4-amino-benzyl)-carbamic acid *tert*-butyl ester (1.28 g, 5.76 mmol) in 2-propanol (10 mL) was stirred at reflux for 3 hr, cooled, poured into saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica gel, 20% EtOAc in hexane) to give a pale yellow solid (2.32 g). To a solution of the above solid (750 mg, 1.91 mmol) in EtOAc (7 mL) was added 4 M hydrogen chloride in EtOAc (7 mL). The mixture was stirred at ambient

temperature for 2 hr, concentrated to give a white solid. To a suspension of the above solid in CH_2Cl_2 (5 mL) was added diisopropylethylamine (730 μL, 4.19 mmol). The mixture was cooled on an ice-bath and a solution of 4-bromo-2-trifluoromethoxy-benzenesulfonyl chloride (777 mg, 2.29 mmol) in CH_2Cl_2 (2 mL) was added dropwise. The reaction mixture was stirred on an ice-bath for 9 hr, poured into saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by medium-pressure liquid chromatography (NH-silica gel, 20% EtOAc in hexane) to give 4-bromo-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-benzyl]-2-trifluoromethoxy-benzenesulfonamide (519 mg, 56%) as a pale yellow solid.

ESI MS m/e 618, M + Na^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (t, J = 9.0 Hz, 2 H), 7.64 (d, J = 8.6 Hz, 2 H), 7.48-7.61 (m, 4 H), 6.98-7.20 (m, 4 H), 4.96 (brs, 1 H),4.13 (s, 2 H), 3.34 (s, 6 H).

Example 27



4-Bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-benzyl}-2-trifluoromethoxy-benzenesulfonamide

Step A: Synthesis of (4-aminomethyl-benzyl)-carbamic acid *tert*-butyl ester.

To a solution of 4-aminomethyl-benzylamine (15.0 g, 110 mmol) in $CHCl_3$ (85 mL) was added a solution of $(Boc)_2O$ (3.03 g, 13.9 mmol) in $CHCl_3$ (45 mL) dropwise over 3.5 hr. The reaction mixture was stirred at ambient temperature for 13 hr, and concentrated. After dissolution with H_2O, the aqueous layer was extracted with EtOAc (three times). The combined organic layer was washed with H_2O (three times), dried over $MgSO_4$, filtered, and concentrated to give (4-aminomethyl-benzyl)-carbamic acid *tert*-butyl ester (3.20 g, 12%) as a white solid.

ESI MS m/e 237, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21-7.30 (m, 4 H), 4.86-5.02 (m, 1 H), 4.29 (d, J = 5.8 Hz, 2 H), 3.84 (s, 2 H), 1.46 (s, 9 H).

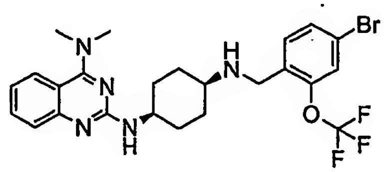
Step B: Synthesis of {4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-benzyl}-carbamic acid *tert*-butyl ester.

Using the procedure for the step G of example 1, the title compound was obtained. ESI MS m/e 408, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, J = 8.2 Hz, 1 H), 7.47-7.55 (m, 2 H), 7.37 (d, J = 8.0 Hz, 2 H), 7.24 (d, J = 8.0 Hz, 2 H), 7.05-7.10 (m, 1 H), 5.35-5.45 (m, 1 H), 4.90-5.04 (m, 1 H), 4.72 (d, J = 5.8 Hz, 2 H), 4.31 (d, J = 5.8 Hz, 2 H), 3.27 (s, 6 H), 1.49 (s, 9 H).

Step C: Synthesis of 4-bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-benzyl}-2-trifluoromethoxy-benzenesulfonamide.

Using the procedure for the step H of example 1, the title compound was obtained. ESI MS m/e 610, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (d, J = 8.4 Hz, 2 H), 7.44-7.54 (m, 4 H), 7.29 (d, J = 7.9 Hz, 2 H), 7.11 (d, J = 8.1 Hz, 2 H), 7.06 (ddd, J = 8.3, 6.3, 2.0 Hz, 1 H), 4.67 (d, J = 5.9 Hz, 2 H), 4.15 (s, 2 H), 3.26 (s, 6 H).

Example 28



***cis*-N^2-[4-(4-Bromo-2-trifluoromethoxy-benzylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine**

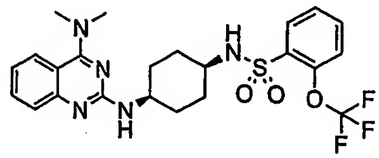
Step A: Synthesis of *cis*-N^2-[4-(4-bromo-2-trifluoromethoxy-benzylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine.

Using the procedure for the step B of example 15, the title compound was obtained.

ESI MS m/e 560, M + Na$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (dd, J = 7.9, 0.9 Hz, 1 H),

7.36-7.51 (m, 5 H), 7.01 (ddd, J = 8.3, 6.4, 1.9 Hz, 1 H), 4.95-5.18 (m, 1 H), 4.08-4.22 (m, 1 H), 3.81 (s, 2 H), 3.25 (s, 6 H), 2.55-2.70 (m, 1 H), 1.65-1.90 (m, 6 H), 1.29-1.65 (m, 2 H).

Example 29

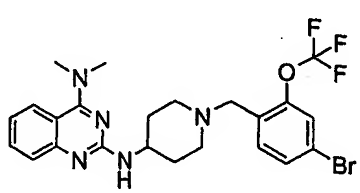


***cis*-*N*-[4-(4-Dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-2-trifluoromethoxy-benzenesulfonamide**

Step A: Synthesis of *cis*-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-2-trifluoromethoxy-benzenesulfonamide.

Using the procedure for the step A of example 20, the title compound was obtained. ESI MS m/e 532, M + Na^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (dd, J = 8.1, 1.9 Hz, 1 H), 7.81 (dd, J = 8.4, 1.4 Hz, 1 H), 7.36-7.66 (m, 5 H), 7.03 (ddd, J = 8.3, 6.7, 1.5 Hz, 1 H), 4.72-5.07 (m, 2 H) , 3.95-4.10 (m, 1 H), 3.32-3.48 (m, 1 H), 3.25 (s, 6 H), 1.37-2.17 (m, 8 H).

Example 30



***N*^{2}-[1-(4-Bromo-2-trifluoromethoxy-benzyl)-piperidin-4-yl]-*N*^{4},*N*^{4}-dimethyl-quinazoline-2,4-diamine**

Step A: Synthesis of *N*^{2}-(1-benzyl-piperidin-4-yl)-*N*^{4},*N*^{4}-dimethyl-quinazoline-2,4-diamine.

Using the procedure for the step G of example 1, the title compound was obtained. ESI MS m/e 362, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, J = 7.6 Hz, 1 H), 7.20-7.52 (m, 7 H), 6.97-7.05 (m, 1 H), 4.74-4.90 (m, 1 H), 3.90-4.05 (m, 1 H), 3.53 (s, 2 H), 3.26 (s, 6 H), 2.78-2.90 (m, 2 H), 2.02-2.24 (m, 4 H), 1.48-1.62 (m, 2 H).

Step B: Synthesis of N^4,N^4-dimethyl-N^2-piperidin-4-yl-quinazoline-2,4-diamine.

To a solution of N^2-(1-benzyl-piperidin-4-yl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine (1.80 g, 4.98 mmol) in MeOH (18 mL) was added 20% $Pd(OH)_2$ (360 mg). The mixture was stirred at 50 °C under hydrogen atmosphere for 3 days, filtered through a pad of celite, and concentrated to give N^4,N^4-dimethyl-N^2-piperidin-4-yl-quinazoline-2,4-diamine (1.33 g, 99%) as a pale yellow solid.

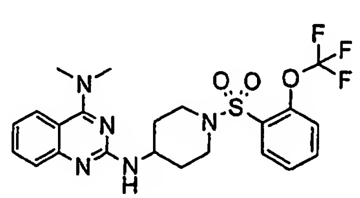
ESI MS m/e 272, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, J = 8.6 Hz, 1 H), 7.43-7.62 (m, 2 H), 7.15 (t, J = 8.2 Hz, 1 H), 4.12-4.29 (m, 1 H), 3.29-3.47 (m, 2 H), 3.37 (s, 6 H), 2.96-3.12 (m, 2 H), 2.20-2.34 (m, 2 H), 1.79-1.97 (m, 2 H).

Step C: Synthesis of N^2-[1-(4-bromo-2-trifluoromethoxy-benzyl)-piperidin-4-yl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine.

Using the procedure for the step B of example 15, the title compound was obtained.

ESI MS m/e 546, M + Na$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (dd, J = 8.7, 0.9 Hz, 1 H), 7.34-7.54 (m, 5 H), 7.01 (ddd, J = 8.3, 6.6, 1.6 Hz, 1 H), 4.76-4.95 (m, 1 H), 3.87-4.06 (m, 1 H), 3.52 (s, 2 H), 3.25 (s, 6 H), 2.71-2.86 (m, 2 H), 2.17-2.33 (m, 2 H), 1.97-2.12 (m, 2 H), 1.44-1.61 (m, 2 H).

Example 31

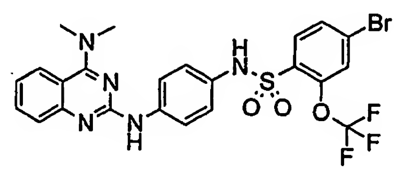


N^4,N^4-Dimethyl-N^2-[1-(2-trifluoromethoxy-benzenesulfonyl)-piperidin-4-yl]-quinazoline-2,4-diamine

Step A: Synthesis of *N*[4],*N*[4]-dimethyl-*N*[2]-[1-(2-trifluoromethoxy-benzenesulfonyl)-piperidin-4-yl]-quinazoline-2,4-diamine.

Using the procedure for the step A of example 20, the title compound was obtained. ESI MS m/e 518, M + Na^+; ^1H NMR (300 MHz, $CDCl_3$) δ 8.02 (dd, J = 7.9, 1.9 Hz, 1 H), 7.81 (dd, J = 8.4, 0.7 Hz, 1 H), 7.34-7.67 (m, 5 H), 7.04 (ddd, J = 8.3, 6.7, 1.5 Hz, 1 H), 4.81 (brs, 1 H), 3.95-4.12 (m, 1 H), 3.78 (d, J = 12.8 Hz, 2 H), 3.25 (s, 6 H), 2.85-3.05 (m, 2 H), 2.05-2.28 (m, 2 H), 1.50-1.71 (m, 2 H).

Example 32



4-Bromo-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-phenyl]-2-trifluoromethoxy-benzenesulfonamide

Step A: Synthesis of [4-(4-dimethylamino-quinazolin-2-ylamino)-phenyl]-carbamic acid *tert*-butyl ester.

Using the procedure for the step G of example 1, the title compound was obtained. ESI MS m/e 402, M + Na^+; ^1H NMR (300 MHz, $CDCl_3$) δ 10.05 (brs, 1 H), 7.94 (d, J = 8.4 Hz, 1 H), 7.50-7.66 (m, 4 H), 7.23-7.38 (m, 3 H), 6.57-6.64 (m, 1 H), 3.48 (s, 6 H), 1.53 (s, 9 H).

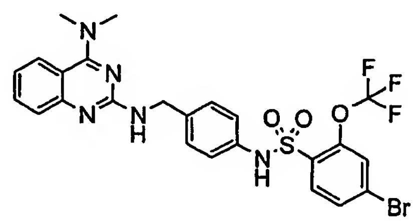
Step B: Synthesis of 4-bromo-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-phenyl]-2-trifluoromethoxy-benzenesulfonamide

To a suspension of [4-(4-dimethylamino-quinazolin-2-ylamino)-phenyl]-carbamic acid *tert*-butyl ester (380 mg, 1.00 mmol) in EtOAc (4 mL) and CH_2Cl_2 (4 mL) was added 4 M hydrogen chloride in EtOAc (4 mL). The mixture was stirred at ambient temperature for 4 hr and concentrated to give a white solid. The solid was alkalized with saturated aqueous $NaHCO_3$, filtered, washed with H_2O and hexane, and dried at 50 °C under reduced

pressure. To a solution of 4-bromo-2-trifluoromethoxy-benzenesulfonyl chloride (680 mg, 2.00 mmol) in CH_2Cl_2 (30 mL) was added PVP (8 mL). To the resulting suspension was added a solution of the above solid in CH_2Cl_2 (5 mL). The mixture was stirred at ambient temperature for 10.5 hr and filtered. The filtrate was washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$, filtered, concentrated, and purified by medium-pressure liquid chromatography (NH-silica gel, EtOAc) to give a solid . The solid was washed with Et_2O and dried at 50 °C under reduced pressure to give 4-bromo-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-phenyl]-2-trifluoromethoxy-benzenesulfonamide (202 mg, 35%) as a pale yellow solid.

ESI MS m/e 582, M + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, J = 8.4 Hz, 1 H), 7.73 (d, J = 8.4 Hz, 1 H), 7.64 (d, J = 8.9 Hz, 2 H), 7.51-7.58 (m, 3 H), 7.44 (dd, J = 8.4, 1.7 Hz, 1 H), 7.07-7.24 (m, 1 H), 7.02 (d, J = 8.9 Hz, 2 H), 3.32 (s, 6 H).

Example 33



4-Bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-phenyl}-2-trifluoromethoxy-benzenesulfonamide

Step A: Synthesis of [4-(*tert*-butoxycarbonylamino-methyl)-phenyl]-carbamic acid benzyl ester.

To a solution of 4-aminomethyl-phenylamine (3.00 g, 24.6 mmol) in $CHCl_3$ (30 mL) was added triethylamine (2.61 g, 25.8 mmol). After cooling on an ice-bath, $(Boc)_2O$ (5.63 g, 25.8 mmol) was added dropwise. The reaction mixture was stirred at ambient temperature for 55 min and poured into saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times) and the combined organic layer was dried over $MgSO_4$, filtered, and concentrated to give a pale yellow oil. To a solution of the above oil in $CHCl_3$ (30 mL) was added diisopropylethylamine (3.33 g, 25.8 mmol). The resulting solution was cooled to 4 °C and ZCl (4.40 g, 25.8 mmol) was added below 10 °C over 5 min. The reaction mixture was stirred at ambient temperature for 12 hr, and poured into

saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (silica gel, 2% MeOH in $CHCl_3$) to give [4-(*tert*-butoxycarbonylamino-methyl)-phenyl]-carbamic acid benzyl ester (2.64 g, 30%) as a white solid.

ESI MS m/e 379, M + Na^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.11-7.44 (m, 9 H), 6.76 (brs, 1 H), 5.19 (s, 2 H), 4.81 (brs, 1 H), 4.25 (d, J = 5.1 Hz, 2 H), 1.45 (s, 9 H).

Step B: Synthesis of (4-aminomethyl-phenyl)-carbamic acid benzyl ester hydrochloride.

A solution of [4-(*tert*-butoxycarbonylamino-methyl)-phenyl]-carbamic acid benzyl ester (1.25 g, 3.51 mmol) in EtOAc (20 mL) was cooled on an ice-bath and 4 M hydrogen chloride in EtOAc (20 mL) was added. The mixture was stirred at ambient temperature for 20 min. The precipitate was collected by filtration, washed with EtOAc, and dried under reduced pressure to give (4-aminomethyl-phenyl)-carbamic acid benzyl ester hydrochloride (957 mg, 93%) as a white solid.

ESI MS m/e 279, M + Na^+; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.90 (s, 1 H), 8.37 (brs, 3 H), 7.29-7.55 (m, 9 H), 5.15 (s, 2 H), 3.85-4.01 (m, 2 H).

Step C: Synthesis of {4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-phenyl}-carbamic acid benzyl ester.

Using the procedure for the step C of example 3, the title compound was obtained. ESI MS m/e 428, M + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, J = 7.5 Hz, 1 H), 7.25-7.52 (m, 11 H), 6.98-7.07 (m, 1 H), 6.74 (brs, 1 H), 5.28 (brs, 1 H), 5.19 (s, 2 H), 4.65 (d, J = 5.9 Hz, 2 H), 3.25 (s, 6 H).

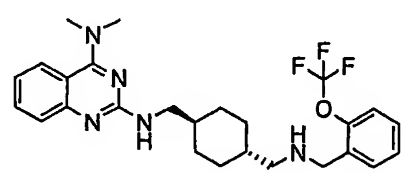
Step D: Synthesis of 4-bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-phenyl}-2-trifluoromethoxy-benzenesulfonamide.

To a solution of {4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-phenyl}-carbamic acid benzyl ester (318 mg, 0.744 mmol) in MeOH (3 mL) was added 5% Pd/C (30 mg). The mixture was stirred at 50 °C under hydrogen atmosphere for 41.5 hr, filtered through a pad of celite, and concentrated. To a solution of 4-bromo-2-trifluoromethoxy-benzenesulfonyl chloride (505 mg, 1.49 mmol) in CH_2Cl_2 (12 mL) was added PVP (6 mL).

To the resulting suspension was added a solution of the above residue in CH_2Cl_2 (10 mL). The mixture was stirred at ambient temperature for 1.5 days, filtered, poured into saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by medium-pressure liquid chromatography (NH-silica gel, 33% EtOAc in hexane) to give 4-bromo-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-phenyl}-2-trifluoromethoxy-benzenesulfonamide (330 mg, 74%) as a pale brown solid.

ESI MS m/e 596, M + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.4 Hz, 1 H), 7.77 (d, *J* = 8.4 Hz, 1 H), 7.41-7.60 (m, 4 H), 7.22 (d, *J* = 8.6 Hz, 2 H), 7.08-7.18 (m, 1 H), 6.99 (d, *J* = 8.6 Hz, 2 H), 4.56 (d, *J* = 5.6 Hz, 2 H), 3.34 (s, 6 H).

Example 34



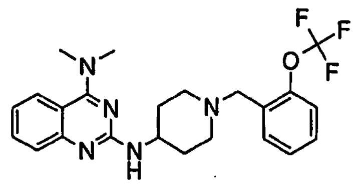
***trans*-*N*^{4},*N*^{4}-Dimethyl-*N*^{2}-{4-[(2-trifluoromethoxy-benzylamino)-methyl]-cyclohexylmethyl}-quinazoline-2,4-diamine**

Step A: Synthesis of *trans*-*N*^{4},*N*^{4}-dimethyl-*N*^{2}-{4-[(2-trifluoromethoxy-benzylamino)-methyl]-cyclohexylmethyl}-quinazoline-2,4-diamine.

Using the procedure for the step B of example 15, the title compound was obtained.

ESI MS m/e 510, M + Na^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.2 Hz, 1 H), 7.39-7.57 (m, 3 H), 7.15-7.35 (m, 3 H), 7.02 (ddd, *J* = 8.3, 6.0, 2.2 Hz, 1 H), 3.83 (s, 2 H), 3.35 (t, *J* = 6.3 Hz, 2 H), 3.27 (s, 6 H), 2.45 (d, *J* = 6.5 Hz, 2 H), 1.69-2.04 (m, 4 H), 1.37-1.69 (m, 2 H), 0.84-1.12 (m, 4 H).

Example 35



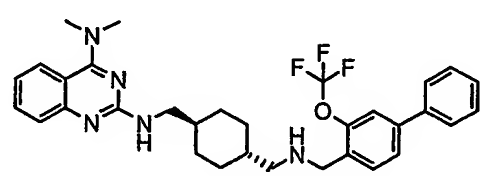
***N*⁴,*N*⁴-Dimethyl-*N*²-[1-(2-trifluoromethoxy-benzyl)-piperidin-4-yl]-quinazoline-2,4-diamine**

Step A: Synthesis of *N*⁴,*N*⁴-dimethyl-*N*²-[1-(2-trifluoromethoxy-benzyl)-piperidin-4-yl]-quinazoline-2,4-diamine.

Using the procedure for the step B of example 15, the title compound was obtained.

ESI MS m/e 468, M + Na^+ ; ^1H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, J = 7.8 Hz, 1 H), 7.37-7.63 (m, 3 H), 7.17-7.35 (m, 3 H), 7.02 (ddd, J = 8.3, 6.4, 1.9 Hz, 1 H), 5.12 (brs, 1 H), 3.86-4.07 (m, 1 H), 3.60 (s, 2 H), 3.26 (s, 6 H), 2.74-2.94 (m, 2 H), 2.18-2.37 (m, 2 H), 1.98-2.15 (m, 2 H), 1.45-1.69 (m, 2 H).

Example 36



2HCl

***trans*-*N*⁴,*N*⁴-Dimethyl-*N*²-(4-{[(3-trifluoromethoxy-biphenyl-4-ylmethyl)-amino]-methyl}-cyclohexylmethyl)-quinazoline-2,4-diamine dihydrochloride**

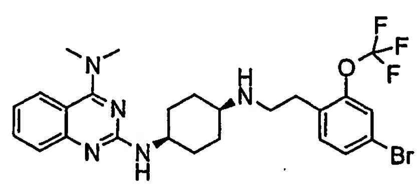
Step A: Synthesis of *trans*-*N*⁴,*N*⁴-dimethyl-*N*²-(4-{[(3-trifluoromethoxy-biphenyl-4-ylmethyl)-amino]-methyl}-cyclohexylmethyl)-quinazoline-2,4-diamine-dihydrochloride.

To a solution of *trans*-*N*²-{4-[(4-bromo-2-trifluoromethoxy-benzylamino)-methyl]-cyclohexylmethyl}-*N*⁴,*N*⁴-dimethyl-quinazoline-2,4-diamine obtained in step B of example

15 (300 mg, 0.529 mol) in toluene (6.6 mL) were added MeOH (2.2 mL), 2 M aqueous K_2CO_3 (2.2 mL), phenylboronic acid (77 mg, 0.635 mmol), and tetrakis (triphenylphosphine) palladium (61 mg, 0.053 mmol). The reaction mixture was stirred at 130 °C for 12 hr. The mixture was poured into water, and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated and, purified by flash chromatography (NH-silica gel, 33% $CHCl_3$ in hexane and silica gel, 9% MeOH in $CHCl_3$) to give pale yellow oil. To a solution of above oil in EtOAc (2 mL) was added 4 M hydrogen chloride in EtOAc (0.1 mL). The mixture was stirred at ambient temperature for 20 min and concentrated. A solution of the residue in Et_2O (2 mL) was stirred at ambient temperature for 30 min. The precipitate was collected by filtration, washed with Et_2O, and dried under reduced pressure to give *trans*-N^4,N^4-dimethyl-N^2-(4-{[(3-trifluoromethoxy-biphenyl-4-ylmethyl)-amino]-methyl}-cyclohexylmethyl)-quinazoline-2,4-diamine dihydrochloride (70 mg, 21%) as a white solid.

ESI MS m/e 564, M (free) + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.27 (s, 1 H), 9.96 (brs, 2 H), 8.17-8.32 (m, 2 H), 7.89 (d, J = 7.9 Hz, 1 H), 7.34-7.64 (m, 9 H), 7.20 (t, J = 7.7 Hz, 1 H), 4.29 (brs, 2 H), 3.50 (s, 6 H), 3.28 (t, J = 6.1 Hz, 2 H), 2.69 (brs, 2 H), 1.79-2.11 (m, 4 H), 1.44-1.68 (m, 2 H), 0.91-1.16 (m, 4 H).

Example 37



2HCl

***cis*-N^2-{4-[2-(4-Bromo-2-trifluoromethoxy-phenyl)-ethylamino]-cyclohexyl}-N^4,N^4,-dimethyl-quinazoline-2,4-diamine dihydrochloride**

Step A: Synthesis of (4-bromo-2-trifluoromethoxy-phenyl)-acetaldehyde.

To a suspension of (methoxymethyl) triphenylphosphonium chloride (5.29 g, 14.9 mol) in Et_2O (50 mL) was added 1.8 M phenyl lithium in 30% Et_2O in cyclohexane (8.58 mL, 15.5 mmol). The mixture was stirred at ambient temperature for 10 min. To the

reaction mixture was added 4-bromo-2-trifluoromethoxy-benzaldehyde (4 g, 14.9 mmol) in Et_2O (18 mL). The mixture was stirred at ambient temperature for 4 hr, filtrated, and concentrated. To the above residue was added 10% H_2SO_4 in AcOH (40 mL). The mixture was stirred at ambient temperature for 90 min. The solution was poured into H_2O, and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was washed with saturated aqueous $NaHCO_3$, washed with brine, dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (silica gel, 9% EtOAc in hexane) to give (4-bromo-2-trifluoromethoxy-phenyl)-acetaldehyde (1.25 g, 30 %) as a pale brown oil.

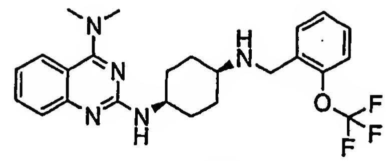
ESI MS m/e 284, M + H^+; ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.74 (t, J = 1.5 Hz, 1 H), 7.41-7.51 (m, 2 H), 7.16 (d, J = 8.4 Hz, 1 H), 3.75 (d, J = 1.5 Hz, 2 H).

Step B: Synthesis of *cis-N*^{2}-{4-[2-(4-bromo-2-trifluoromethoxy-phenyl)-ethylamino] -cyclohexyl}-*N*^{4},*N*^{4}-dimethyl-quinazoline-2,4-diamine dihydrochloride.

To a suspension of *cis-N*^{2}-(4-amino-cyclohexyl)-*N*^{4},*N*^{4}-dimethyl-quinazoline-2,4-diamine obtained in step C of example 9 (300 mg, 1.05 mmol) in CH_2Cl_2 (3 mL) were added (4-bromo-2-trifluoromethoxy-phenyl)-acetaldehyde (357 mg, 1.26 mmol), AcOH (76 mg, 1.26 mmol), and $NaBH(OAc)_3$ (334 mg, 1.57 mmol). The reaction mixture was stirred at ambient temperature for 4.5 hr. The reaction was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica gel, 50% EtOAc in hexane) to give a pale yellow solid. To a solution of above solid in EtOAc (0.8 mL) was added 4 M hydrogen chloride in EtOAc (0.25 mL). The mixture was stirred at ambient temperature for 30 min and concentrated. A solution of the residue in Et_2O (2 mL) was stirred at ambient tempareture for 30 min. The precipitate was collected by filtration, washed with Et_2O, and dried under reduced pressure to give *cis-N*^{2}-{4-[2-(4-bromo-2-trifluoromethoxy-phenyl)-ethylamino]-cyclohexyl}-*N*^{4},*N*^{4}-dimethyl-quinazoline-2,4-diamine dihydrochloride (161 mg, 25%) as a white solid.

ESI MS m/e 552, M (free)$^+$; ^{1}H NMR (200 MHz, $CDCl_3$) δ 12.66 (brs, 1 H), 9.91 (brs, 2 H), 8.71 (brs, 1 H), 7.93 (d, J = 6.6 Hz, 1 H), 7.19-7.77 (m, 6 H), 4.31 (brs, 1 H), 3.54 (s, 6 H), 3.09-3.78 (m, 5 H), 2.00-2.48 (m, 6 H), 1.62-1.96 (m, 2 H).

Example 38



2HCl

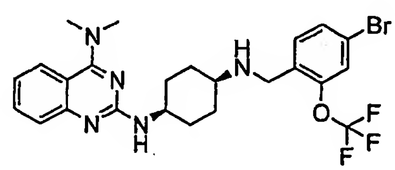
***cis*-N^4,N^4-Dimethyl-N^2-[4-(2-trifluoromethoxy-benzylamino)-cyclohexyl]-quinazoline-2,4-diamine dihydrochloride**

Step A: Synthesis of *cis*-N^4,N^4-dimethyl-N^2-[4-(2-trifluoromethoxy-benzylamino)-cyclohexyl]-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step B of example 37, the title compound was obtained.

ESI MS m/e 460, M (free) + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.68 (d, J = 7.6 Hz, 1 H), 8.19-8.33 (m, 1 H), 7.95 (d, J = 8.2 Hz, 1 H), 7.66 (t, J = 7.7 Hz, 1 H), 7.47 (d, J = 8.1 Hz, 1 H), 7.18-7.44 (m, 4 H), 4.35 (s, 2 H), 4.15-4.47 (m, 1 H), 3.53 (s, 6 H), 3.02-3.31 (m, 1 H), 1.95-2.37 (m, 6 H), 1.51-1.85 (m, 2 H).

Example 39



2HCl

***cis*-N^2-[4-(4-Bromo-2-trifluoromethoxy-benzylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride**

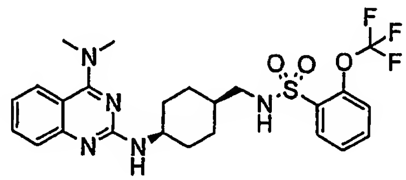
Step A: Synthesis of *cis*-N^2-[4-(4-bromo-2-trifluoromethoxy-benzylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step A of example 2, the title compound was obtained.

ESI MS m/e 538, M (free) + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.77 (d, J = 7.5 Hz, 1 H), 8.11 (d, J = 8.4 Hz, 1 H), 7.92 (d, J = 8.6 Hz, 1 H), 7.67 (t, J = 7.7 Hz, 1 H), 7.41-7.53 (m,

2 H), 7.37 (s, 1 H), 7.28 (t, $J = 7.8$ Hz, 1 H), 4.19-4.40 (m, 1 H), 4.26 (s, 2 H), 3.52 (s, 7 H), 3.07-3.25 (m, 1 H), 2.00-2.39 (m, 6 H), 1.61-1.88 (m, 2 H).

Example 40



HCl

***cis-N*-[4-(4-Dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-trifluoromethoxy-benzenesulfonamide hydrochloride**

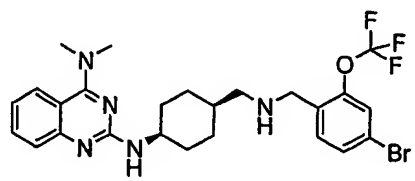
Step A: Synthesis of *cis-N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-trifluoromethoxy-benzenesulfonamide hydrochloride.

To a solution of *cis*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-carbamic acid benzyl ester obtained in step B of example 24 (4.57 g, 10.5 mmol) in MeOH (46 mL) was added 5% Pd/C (460 mg). The mixture was stirred at 50 °C under hydrogen atmosphere for 3 days, filtered, and concentrated to give a white solid (3.79 g). To a solution of the above solid (500 mg, 1.67 mmol) in CH_2Cl_2 (5 mL) was added diisopropylethylamine (440 µL, 2.53 mmol). The mixture was cooled on an ice-bath and a solution of 2-trifluoromethoxy-benzenesulfonyl chloride (457 mg, 1.75 mmol) in CH_2Cl_2 (2 mL) was added dropwise. The reaction mixture was stirred on an ice-bath for 10 hr. The reaction was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, purified by medium-pressure liquid chromatography (NH-silica gel, 33% EtOAc in hexane), and concentrated. To a solution of the residue in EtOAc (1 mL) was added 4 M hydrogen chloride in EtOAc (5 mL). The reaction mixture was stirred at ambient temperature for 30 min, and concentrated. A solution of the residue in Et_2O (10 mL) was stirred at ambient temperature for 1 hr and the precipitate was collected by filtration to give *cis-N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-trifluoromethoxy-benzenesulfonamide hydrochloride (262 mg, 34%) as a white solid.

ESI MS m/e 524, M (free) + H^+; ^1H NMR (300 MHz, $CDCl_3$) δ 13.18 (s, 1 H), 8.75 (d, $J =$

7.6 Hz, 1 H), 8.03 (dd, J = 8.0, 1.7 Hz, 1 H), 7.89 (d, J = 8.2 Hz, 1 H), 7.56-7.71 (m, 2 H), 7.34-7.55 (m, 3 H) , 7.24 (t, J = 7.5 Hz, 1 H), 4.99 (t, J = 6.5 Hz, 1 H), 4.20-4.33 (m, 1 H), 3.50 (s, 6 H), 2.88 (t, J = 6.3 Hz, 2 H), 1.78-1.99 (m, 2 H), 1.38-1.77 (m, 7 H).

Example 41



2HCl

***cis*-N^2-{4-[(4-Bromo-2-trifluoromethoxy-benzylamino)-methyl]-cyclohexyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride**

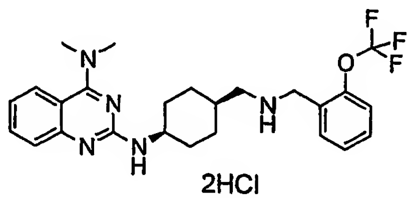
Step A: Synthesis of *cis*-N^2-{4-[(4-bromo-2-trifluoromethoxy-benzylamino)-methyl]-cyclohexyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride.

To a solution of *cis*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-carbamic acid benzyl ester obtained in step B of example 24 (4.57 g, 10.5 mmol) in MeOH (46 mL) was added 5% Pd/C (460 mg). The mixture was stirred at 50 °C under hydrogen atmosphere for 3 days, filtered, and concentrated to give a colorless solid (3.79 g). To a solution of the above solid (500 mg, 1.67 mmol) in CH_2Cl_2 (5 mL) were added 4-bromo-2-trifluoromethoxy-benzaldehyde obtained in step A of example 13 (449 mg, 1.67 mmol), AcOH (100 mg, 1.67 mmol), and $NaBH(OAc)_3$ (531 g, 2.51 mmol). The reaction mixture was stirred at ambient temperature with $CaCl_2$ tube for 9 hr, poured into saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, purified by medium-pressure liquid chromatography (NH-silica gel, 25% EtOAc in hexane), and concentrated. To a solution of the residue in EtOAc (1 mL) was added 4 M hydrogen chloride in EtOAc (5 mL). The reaction mixture was stirred at ambient temperature for 30 min, and concentrated. A solution of the residue in Et_2O (10 mL) was stirred at ambient temperature for 1 hr and the precipitate was collected by filtration to give *cis*-N^2-{4-[(4-bromo-2-trifluoromethoxy-benzylamino)-methyl]-cyclohexyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride (147 mg, 34%) as a white solid.

ESI MS m/e 552, M (free) + H^+; ^1H NMR (300 MHz, $CDCl_3$) δ 12.62 (s, 1 H), 10.07 (brs,

2 H), 8.66 (d, J = 7.6 Hz, 1 H), 8.22 (d, J = 8.4 Hz, 1 H), 7.90 (d, J = 8.4 Hz, 1 H), 7.65 (t, J = 7.6 Hz, 1 H), 7.52 (dd, J = 8.3, 1.8 Hz, 1 H), 7.33-7.48 (m, 2 H), 7.26 (t, J = 7.5 Hz, 1 H), 4.11-4.36 (m, 3 H), 3.51 (s, 6 H), 2.76-2.97 (m, 2 H), 1.51-2.27 (m, 9 H).

Example 42



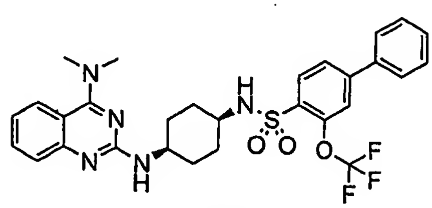
2HCl

***cis*-N^4,N^4-Dimethyl-N^2-{4-[(2-trifluoromethoxy-benzylamino)-methyl]-cyclohexyl}-quinazoline-2,4-diamine dihydrochloride**

Step A: Synthesis of *cis*-N^4,N^4-dimethyl-N^2-{4-[(2-trifluoromethoxy-benzylamino)-methyl]-cyclohexyl}-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step A of example 41, the title compound was obtained. ESI MS m/e 474, M (free) + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.81 (s, 1 H), 9.97 (brs, 1 H), 8.69 (d, J = 7.5 Hz, 1 H), 8.16-8.28 (m, 1 H), 7.90 (d, J = 8.4 Hz, 1 H), 7.63 (t, J = 7.6 Hz, 1 H), 7.18-7.51 (m, 4 H), 4.31 (brs, 2 H), 4.15-4.30 (m, 1 H), 3.50 (s, 6 H), 2.70-2.94 (m, 2 H), 1.41-2.28 (m, 10 H).

Example 43



HCl

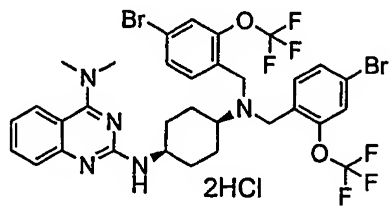
***cis*-3-Trifluoromethoxy-biphenyl-4-sulfonic acid [4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-amide hydrochloride**

Step A: Synthesis of *cis*-3-trifluoromethoxy-biphenyl-4-sulfonic acid [4-(4-

dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-amide hydrochloride.

Using the procedure for the step A of example 36, the title compound was obtained. ESI MS m/e 586, M (free) + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.20 (brs, 1 H), 8.82 (d, *J* = 8.1 Hz, 1 H), 8.09 (d, *J* = 8.6 Hz, 1 H), 7.88 (d, *J* = 7.8 Hz, 1 H), 7.40-7.73 (m, 8 H), 7.25 (t, *J* = 8.4 Hz, 1 H), 5.41 (d, *J* = 8.6 Hz, 1 H), 4.07-4.22 (m, 1 H), 3.49 (s, 6 H), 3.37-3.62 (m, 1 H), 1.57-2.01 (m, 8 H).

Example 44



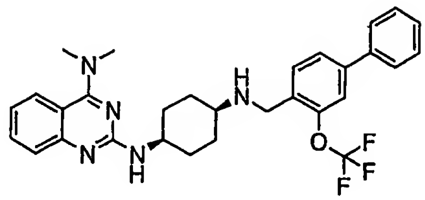
***cis*-N^2-{4-[Bis-(4-bromo-2-trifluoromethoxy-benzyl)-amino]-cyclohexyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride**

Step A: Synthesis of *cis*-N^2-{4-[bis-(4-bromo-2-trifluoromethoxy-benzyl)-amino]-cyclohexyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step B of example 37, the title compound was obtained.

ESI MS m/e 790, M (free) + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.50-12.82 (m, 2 H), 9.50-9.69 (m, 1 H), 8.39 (d, *J* = 8.1 Hz, 2 H), 7.91 (d, *J* = 8.1 Hz, 1 H), 7.66 (t, *J* = 7.8 Hz, 1 H), 7.48 (t, *J* = 8.7 Hz, 2 H), 7.07-7.43 (m, 4 H), 4.06-4.67 (m, 5 H), 3.51 (s, 6 H), 2.97-3.27 (m, 1 H), 2.21-2.59 (m, 4 H), 1.89-2.17 (m, 2 H), 1.36-1.82 (m, 2 H)

Example 45



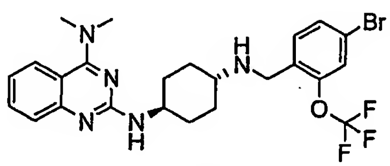
2HCl

***cis*-N^4,N^4-Dimethyl-N^2-{4-[(3-trifluoromethoxy-biphenyl-4-ylmethyl)-amino]-cyclohexyl}-quinazoline-2,4-diamine dihydrochloride**

Step A: Synthesis of *cis*-N^4,N^4-dimethyl-N^2-{4-[(3-trifluoromethoxy-biphenyl-4-ylmethyl)-amino]-cyclohexyl}-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step A of example 43, the title compound was obtained. ESI MS m/e 536, M (free) + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.63 (brs, 1 H), 10.07 (brs, 2 H), 8.68 (d, J = 7.3 Hz, 1 H), 8.33 (d, J = 8.1 Hz, 1 H), 7.90 (d, J = 8.4 Hz, 1 H), 7.17-7.68 (m, 10 H), 4.40 (s, 2 H), 4.19-4.33 (m, 1 H) , 3.50 (s, 6 H), 3.16-3.37 (m, 1 H), 2.03-2.48 (m, 6 H), 1.64-1.88 (m, 2 H).

Example 46



2HCl

***trans*-N^2-[4-(4-Bromo-2-trifluoromethoxy-benzylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride**

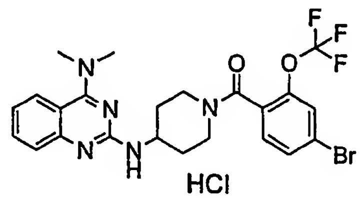
Step A: Synthesis of *trans*-N^2-[4-(4-bromo-2-trifluoromethoxy-benzylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step B of example 37, the title compound was obtained.

ESI MS m/e 537, M (free)$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.00 (brs, 1 H), 10.08 (brs, 2 H), 8.40 (d , J = 7.2 Hz, 1 H), 8.05 (d, J = 8.2 Hz, 1 H), 7.91 (d , J = 8.4 Hz, 1 H), 7.65 (t,

$J = 7.7$ Hz, 1 H), 7.38-7.57 (m, 3 H), 7.26 (t, $J = 7.6$ Hz, 1 H), 4.17 (s, 2 H), 3.83-4.06 (m, 1 H), 3.53 (s, 6 H), 2.76-2.99 (m, 1 H), 2.09-2.46 (m, 4 H), 1.74-2.00 (m, 2 H), 1.28-1.58 (m, 2 H).

Example 47



1-(4-Bromo-2-trifluoromethoxy-phenyl)-1-[4-(4-dimethylamino-quinazolin-2-ylamino)-piperidin-1-yl]-methanone hydrochloride

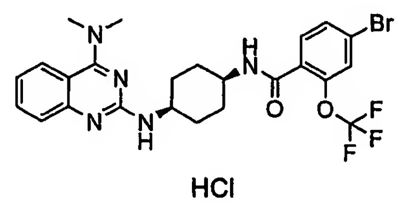
Step A: Synthesis of (4-bromo-2-trifluoromethoxy-phenyl)-[4-(4-dimethylamino-quinazolin-2-ylamino)-piperidin-1-yl]-methanone hydrochloride.

To a solution of 4-bromo-2-trifluoromethoxy-benzoic acid obtained in step B of example 13 (440 mg, 1.47 mmol) in CH_2Cl_2 (5 mL) were added DMF (1.1 μL, 15 μmol) and $SOCl_2$ (175 μL, 2.09 mmol). The mixture was stirred at reflux for 30 min and concentrated to give acid chloride as a pale yellow oil. To a solution of N^4,N^4-dimethyl-N^2-piperidin-4-yl-quinazoline-2,4-diamine obtained in step B of example 30 (400 mg, 1.47 mmol) in CH_2Cl_2 (4 mL) was added diisopropylethylamine (538 μL, 3.08 mmol). The mixture was cooled at 4 °C and a solution of above acid chloride in CH_2Cl_2 (3 mL) was added below 5 °C. The reaction mixture was stirred at 4 °C for 3 hr. The reaction was quenched with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica gel, 25% EtOAc in hexane) to give a pale yellow oil. To a solution of above oil in EtOAc (1 mL) was added 4 M hydrogen chloride in EtOAc (0.26 mL). The mixture was stirred at ambient temperature for 50 min and concentrated. A solution of the residue in Et_2O (5 mL) was stirred at ambient tempareture for 30 min. The precipitate was collected by filtration, washed with Et_2O, and dried under reduced pressure to give (4-bromo-2-trifluoromethoxy-phenyl)-[4-(4-dimethylamino-quinazolin-2-ylamino)-piperidin-1-yl]-methanone hydrochloride (126

mg, 16%) as a white solid.

ESI MS m/e 538, M (free) + H$^+$; ^{1}H NMR (200 MHz, $CDCl_3$) δ 13.35 (brs, 1 H), 9.06 (d, J = 7.5 Hz, 1 H), 7.93 (d, J = 8.4 Hz, 1 H), 7.67 (dt, J = 7.7, 0.9 Hz, 1 H), 7.43-7.61 (m, 3 H), 7.18-7.41 (m, 2 H), 4.00-4.44 (m, 2 H), 3.54 (s, 6 H), 3.03-3.78 (m, 3 H), 1.52-2.24 (m, 4 H).

Example 48

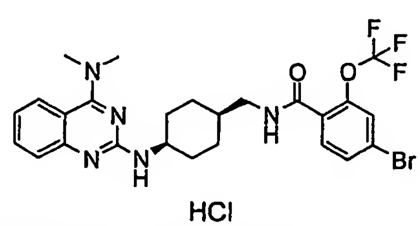


cis-4-Bromo-_N_-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-2-trifluoromethoxy-benzamide dihydrochloride

Step A: Synthesis of 4-bromo-_N_-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-2-trifluoromethoxy-benzamide dihydrochloride.

Using the procedure for the step A of example 47, the title compound was obtained. ESI MS m/e 551, M (free)$^+$; ^{1}H NMR (200 MHz, $CDCl_3$) δ 13.24 (brs, 1 H), 8.95 (d, J = 7.9 Hz, 1 H), 7.92 (d, J = 8.4 Hz, 1 H), 7.71 (d, J = 8.4 Hz, 1 H), 7.60-7.67 (m, 1 H), 7.44-7.58 (m, 3 H), 7.20-7.34 (m, 1 H), 6.57 (d, J = 8.4 Hz, 1 H), 4.00-4.41 (m, 2 H), 3.53 (s, 6 H), 1.66-2.04 (m, 8 H).

Example 49

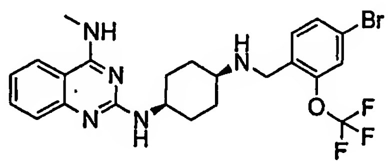


cis-4-Bromo-_N_-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-trifluoromethoxy-benzamide hydrochloride

Step A: Synthesis of 4-bromo-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-trifluoromethoxy-benzamide hydrochloride.

Using the procedure for the step A of example 47, the title compound was obtained. ESI MS m/e 565, M (free)$^+$; ^{1}H NMR (200 MHz, $CDCl_3$) δ 13.20 (brs, 1 H), 8.93 (d, J = 7.9 Hz, 1 H), 7.90 (d, J = 8.4 Hz, 1 H), 7.84 (d, J = 8.4 Hz, 1 H), 7.42-7.70 (m, 4 H), 7.18-7.34 (m, 1 H), 6.87 (t, J = 5.5 Hz, 1 H), 4.34 (brs, 1 H), 3.51 (s, 6 H), 3.43 (t, J = 5.7 Hz, 2 H), 1.52-2.17 (m, 9 H).

Example 50



2HCl

***cis*-N^2-[4-(4-Bromo-2-trifluoromethoxy-benzylamino)-cyclohexyl]-N^4-methyl-quinazoline-2,4-diamine dihydrochloride**

Step A: Synthesis of (2-chloro-quinazolin-4-yl)-methyl-amine.

A solution of 2,4-dichloro-quinazoline obtained in step A of example 1 (125 g, 628 mmol) in THF (1 L) was cooled to 4 °C and 40% aqueous $MeNH_2$ (136 mL, 1.57 mol) was added. The mixture was stirred at ambient temperature for 80 min. The solution was alkalized with saturated aqueous $NaHCO_3$ (pH = 9) and concentrated. The precipitate was collected by filtration, washed with H_2O and hexane, and dried at 80 °C to give (2-chloro-quinazolin-4-yl)-methyl-amine (114 g, 94%) as a white solid.

ESI MS m/e 193, M$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68-7.78 (m, 3 H), 7.39-7.48 (m, 1 H), 6.34 (brs, 1 H), 3.22 (d, J = 4.8 Hz, 3 H).

Step B: Synthesis of *cis*-[4-(4-methylamino-quinazolin-2-ylamino)-cyclohexyl]-carbamic acid *tert*-butyl ester.

Using the procedure for the step G of example 1, the title compound was obtained. ESI MS m/e 372, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36-7.56 (m, 3 H), 7.06 (ddd, J = 8.2, 6.8, 1.3 Hz, 1 H), 5.71 (brs, 1 H), 5.10 (brs, 1 H), 4.45-4.72 (m, 1 H), 4.00-4.26 (m,

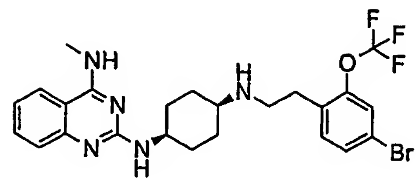
1 H), 3.49-3.76 (m, 1 H), 3.12 (d, $J = 4.8$ Hz, 3 H), 1.50-1.93 (m, 8 H), 1.46 (s, 9 H).

Step C: Synthesis of *cis*-N^2-[4-(4-bromo-2-trifluoromethoxy-benzylamino)-cyclohexyl]-N^4-methyl-quinazoline-2,4-diamine dihydrochloride.

To a suspension of *cis*-[4-(4-methylamino-quinazolin-2-ylamino)-cyclohexyl]-carbamic acid *tert*-butyl ester (1.75 g, 4.71mmol) in EtOAc (5mL) and $CHCl_3$ (10 mL) was added 4 M hydrogen chloride in EtOAc (15 mL). The reaction mixture was stirred at ambient temperature for 2 hr, and concentrated. The residue was alkalized with saturated aqueous $NaHCO_3$ and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated (2.15 g). To a suspension of the above residue (300 mg, 1.11 mmol) in CH_2Cl_2 (3 mL) were added 4-bromo-2-trifluoromethoxy-benzaldehyde obtained in Step A of Example 13 (297 mg, 1.10 mmol), AcOH (66 mg, 1.10 mmol), and $NaBH(OAc)_3$ (351 mg, 1.66 mmol). The reaction mixture was stirred at ambient temperature with $CaCl_2$ tube for 4 hr, poured into saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, purified by medium-pressure liquid chromatography (NH-silica gel, 50% EtOAc in hexane), and concentrated to give a pale yellow oil (91 mg). To a solution of the residue (71 mg) in EtOAc (1 mL) was added 4 M hydrogen chloride in EtOAc (5 mL). The reaction mixture was stirred at ambient temperature for 30 min, and concentrated. A solution of the residue in Et_2O (10 mL) was stirred at ambient temperature for 1 hr and the precipitate was collected by filtration to give *cis*-N^2-[4-(4-bromo-2-trifluoromethoxy-benzylamino)-cyclohexyl]-N^4-methyl-quinazoline-2,4-diamine dihydrochloride (62 mg, 20%) as a white solid.

ESI MS m/e 524, M (free) + H^+ ; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34-7.57 (m, 6 H), 7.05 (ddd, $J = 8.2, 6.8, 1.4$ Hz, 1 H), 5.52 (brs, 1 H), 4.09-4.27 (m, 1 H), 3.82 (s, 2 H), 3.12 (d, $J = 4.8$ Hz, 3 H), 2.57-2.72 (m, 1 H), 1.41-1.94 (m, 8 H).

Example 51



2HCl

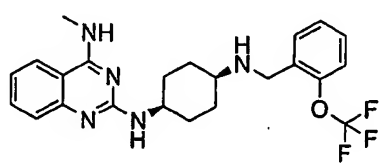
***cis*-N^2-{4-[2-(4-Bromo-2-trifluoromethoxy-phenyl)-ethylamino]-cyclohexyl}-N^4-methyl-quinazoline-2,4-diamine dihydrochloride**

Step A: Synthesis of *cis*-N^2-{4-[2-(4-bromo-2-trifluoromethoxy-phenyl)-ethylamino]-cyclohexyl}-N^4-methyl-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step C of example 50, the title compound was obtained.

ESI MS m/e 538, M (free) + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.18 (brs, 1 H), 9.93 (brs, 3 H), 8.74 (d, J = 6.2 Hz, 1 H), 7.71-7.94 (m, 1 H), 7.60 (t, 1 H, J = 7.7 Hz, 1 H), 7.21-7.45 (m, 5 H), 3.94-4.26 (m, 1 H), 3.35-3.58 (m, 2 H), 3.08-3.33 (m, 3 H), 2.94 (brs, 3 H), 1.64-2.42 (m, 8 H).

Example 52



2HCl

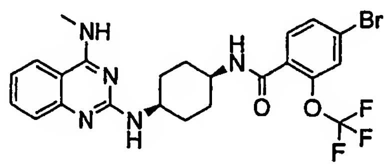
***cis*-N^4-Methyl-N^2-[4-(2-trifluoromethoxy-benzylamino)-cyclohexyl]-quinazoline-2,4-diamine dihydrochloride**

Step A: Synthesis of *cis*-N^4-methyl-N^2-[4-(2-trifluoromethoxy-benzylamino)-cyclohexyl]-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step C of example 50, the title compound was obtained.

ESI MS m/e 446, M (free) + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36-7.56 (m, 4 H), 7.17-7.33 (m, 3 H), 7.04 (ddd, 1 H, J = 8.2, 6.8, 1.4 Hz, 1 H), 5.66 (brs, 1 H), 5.18 (brs, 1 H), 4.11-4.27 (m, 1 H), 3.87 (s, 2 H), 3.10 (d, J = 4.8 Hz, 3 H), 2.60-2.74 (m, 1 H), 1.45-1.95 (m, 8 H).

Example 53



HCl

***cis*-4-Bromo-*N*-[4-(4-methylamino-quinazolin-2-ylamino)-cyclohexyl]-2-trifluoromethoxy-benzamide hydrochloride**

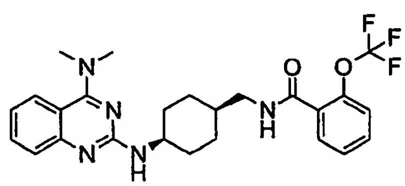
Step A: Synthesis of *cis*-4-bromo-*N*-[4-(4-methylamino-quinazolin-2-ylamino)-cyclohexyl]-2-trifluoromethoxy-benzamide hydrochloride.

To a suspension of *cis*-[4-(4-methylamino-quinazolin-2-ylamino)-cyclohexyl]-carbamic acid *tert*-butyl ester obtained in step B of example 50 (1.75 g, 4.71mmol) in EtOAc (5 mL) and $CHCl_3$ (10 mL) was added 4 M hydrogen chloride in EtOAc (15 mL). The reaction mixture was stirred at ambient temperature for 2 hr, and concentrated. The residue was alkalized with saturated aqueous $NaHCO_3$ and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated. To a solution of 4-bromo-2-trifluoromethoxy-benzoic acid obtained in step B of example 13 (331 mg, 1.16 mmol) in CH_2Cl_2 (5 mL) were added DMF (1 μL, 0.01 mmol) and $SOCl_2$ (120 μL, 1.65 mmol). The mixture was stirred at reflux for 30 min and concentrated to give acid chloride as a pale yellow oil. To a suspension of *cis*-N^2-(4-amino-cyclohexyl)-N^4-methyl-quinazoline-2,4-diamine (300 mg, 1.11 mmol) in CH_2Cl_2 (3 mL) was added diisopropylethylamine (410 μL, 2.35 mmol). The mixture was cooled on an ice-bath and a solution of the above residue in CH_2Cl_2 (3 mL) was added dropwise. The reaction mixture was stirred on an ice-bath for 3.5 hr. The reaction was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by

flash chromatography (NH-silica gel, 50% EtOAc in hexane) to give a pale yellow solid. To a solution of the residue (116 mg) in EtOAc (1 mL) was added 4 M hydrogen chloride in EtOAc (5 mL). The reaction mixture was stirred at ambient temperature for 30 min, and concentrated. A solution of the residue in Et_2O (10 mL) was stirred at ambient temperature for 1 hr and the precipitate was collected by filtration to give 4-bromo-*N*-[4-(4-methylamino-quinazolin-2-ylamino)-cyclohexyl]-2-trifluoromethoxy-benzamide (102 mg, 16%) as a white solid.

ESI MS m/e 538, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.72 (s, 1 H), 8.66 (d, J = 7.1 Hz, 1 H), 8.35 (brs, 1 H), 8.16 (d, J = 7.7 Hz, 1 H), 7.74 (d, J = 8.4 Hz, 1 H), 7.48-7.60 (m, 2 H), 7.40-7.43 (m, 1 H), 7.30 (d, J = 8.4 Hz, 1 H), 7.19 (t, J = 7.8 Hz, 1 H), 6.57 (d, J = 8.1 Hz, 1 H), 4.34 (brs, 1 H), 4.15 (brs, 1 H), 3.22 (d, J = 3.9 Hz, 3 H), 1.90 (m, 8 H).

Example 54



HCl

***cis-N*-[4-(4-Dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-trifluoromethoxy-benzamide hydrochloride**

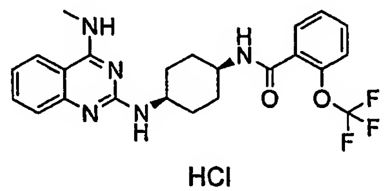
Step A: Synthesis of *cis-N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-trifluoromethoxy-benzamide hydrochloride.

To a solution of *cis*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-carbamic acid benzyl ester obtained in step B of example 24 (4.57 g, 10.5 mmol) in MeOH (46 mL) was added 5% Pd/C (460 mg). The mixture was stirred at 50 °C under hydrogen atmosphere for 3 days, filtered, and concentrated to give a white solid (3.79 g). To a solution of the above solid (300 mg, 1.00 mmol) in CH_2Cl_2 (3 mL) was added triethylamine (280 μL, 2.01 mmol). The mixture was cooled on an ice-bath and a solution of 2-trifluoromethoxy-benzoyl chloride (236 mg, 1.05 mmol) in CH_2Cl_2 (2 mL) was added dropwise. The reaction mixture was stirred on an ice-bath for 5 hr. The reaction was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered,

concentrated, purified by flash chromatography (NH-silica gel, 33% EtOAc in hexane and silica gel, 10% MeOH in $CHCl_3$), and concentrated. To a solution of the residue in EtOAc (1 mL) was added 4 M hydrogen chloride in EtOAc (5 mL). The reaction mixture was stirred at ambient temperature for 30 min, and concentrated. A solution of the residue in Et_2O (10 mL) was stirred at ambient temperature for 1 hr and the precipitate was collected by filtration to give *cis-N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-trifluoromethoxy-benzamide hydrochloride (134 mg, 31%) as a white solid.

ESI MS m/e 510, M (free) + Na^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.29 (s, 1 H), 8.89 (d, J = 7.9 Hz, 1 H), 7.93 (dd, J = 7.7, 1.8 Hz, 1 H), 7.89 (d, J = 8.4 Hz, 1 H), 7.63 (t, J = 7.3 Hz, 1 H), 7.52 (d, J = 7.9 Hz, 1 H), 7.47 (dd, J = 8.1, 1.9 Hz, 1 H), 7.39 (t, J = 7.6 Hz, 1 H), 7.29 (d, J = 9.0 Hz, 1 H), 7.23 (d, J = 7.3 Hz, 1 H), 6.77 (t, J = 5.6 Hz, 1 H), 4.18-4.36 (m, 1 H), 3.51 (s, 6 H), 3.42 (t, J = 6.3 Hz, 2 H), 1.35-2.02 (m, 9 H).

Example 55

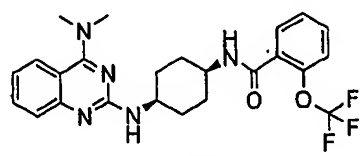


***cis-N*-[4-(4-Methylamino-quinazolin-2-ylamino)-cyclohexyl]-2-trifluoromethoxy-benzamide hydrochloride**

Step A: Synthesis of *cis-N*-[4-(4-methylamino-quinazolin-2-ylamino)-cyclohexyl]-2-trifluoromethoxy-benzamide hydrochloride.

Using the procedure for the step A of example 54, the title compound was obtained. ESI MS m/e 460, M (free) + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.61 (s, 1 H), 8.70 (d, J = 4.4 Hz, 1 H), 8.57 (d, J = 7.6 Hz, 1 H), 8.26 (d, J = 8.1 Hz, 1 H), 7.82 (dd, J = 7.7, 1.8 Hz, 1 H), 7.08-7.57 (m, 6 H), 6.60 (d, J = 8.1 Hz, 1 H), 4.25-4.45 (m, 1 H), 4.01-4.25 (m, 1 H), 3.20 (d, J = 4.5 Hz, 3 H), 1.53-2.18 (m, 8 H).

Example 56



HCl

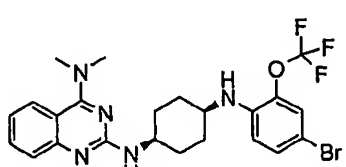
cis-N-[4-(4-Dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-2-trifluoromethoxy-benzamide hydrochloride

Step A: Synthesis of *cis-N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-2-trifluoromethoxy-benzamide hydrochloride.

To a suspension of polymer supported DMAP (2.45 g, 7.35 mmol) in CH_2Cl_2 (6 mL) were added 2-trifluoromethoxy-benzoyl chloride (472 mg, 2.10 mmol) and *cis-N*^{2}-(4-amino-cyclohexyl)-*N*^{4},*N*^{4}-dimethyl-quinazoline-2,4-diamine obtained in step C of example 9 (300 mg, 1.05 mmol). The mixture was stirred at ambient temperature for 24 h, filtered, poured into saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, purified by medium-pressure liquid chromatography (NH-silica gel, 25% EtOAc in hexane), and concentrated. To a solution of the residue in EtOAc (1 mL) was added 4 M hydrogen chloride in EtOAc (10 mL). The reaction mixture was stirred at ambient temperature for 1 hr, and concentrated. A solution of the residue in Et_2O (10 mL) was stirred at ambient temperature for 1 hr and the precipitate was collected by filtration to give *cis-N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-2-trifluoromethoxy-benzamide hydrochloride (145 mg, 27%) as a white solid.

ESI MS m/e 474, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.22 (s, 1 H), 8.88 (d, J = 7.5 Hz, 1 H), 7.90 (d, J = 8.2 Hz, 1 H), 7.79 (dd, J = 7.6, 1.9 Hz, 1 H), 7.64 (t, J = 7.5 Hz, 1 H), 7.52 (d, J = 8.7 Hz, 1 H), 7.47 (dd, J = 8.1, 1.9 Hz, 1 H), 7.37 (dt, J = 7.5, 1.2 Hz, 1 H), 7.20-7.33 (m, 2 H), 6.66 (d, J = 8.4 Hz, 1 H), 4.06-4.36 (m, 2 H), 3.52 (s, 6 H), 1.55-2.21 (m, 8 H).

Example 57



2HCl

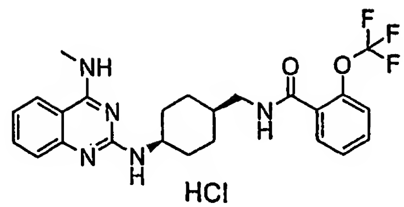
cis-N^2-[4-(4-Bromo-2-trifluoromethoxy-phenylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride

Step A: Synthesis of _cis_-N^2-[4-(4-bromo-2-trifluoromethoxy-phenylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride.

To a glass flask were added 18-crown-6 (647 mg, 2.45 mmol), 4-Bromo-1-iodo-2-trifluoromethoxy-benzene (770 mg, 2.10 mmol), *cis*-N^2-(4-amino-cyclohexyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine obtained in step C of example 9 (500 mg, 1.75 mmol), sodium *tert*-butoxide (235 mg, 2.45 mmol), tris(dibenzylideneacetone)dipalladium (160 mg, 0.175 mmol), (R)-(+)-2,2'-Bis(diphenylphosphino)-1,1'-binaphthyl (160 mg, 0.175 mmol) and THF (3.5 mL). The reaction mixture was stirred at reflux 18 hr. The mixture was filtered through a pad of celite, concentrated, and purified by flash chromatography (NH-silica gel, 33% EtOAc in hexane) to give a pale yellow oil. To a solution of above oil in Et_2O (2 mL) was added 4 M hydrogen chloride in EtOAc (0.3 mL). The mixture was stirred at ambient temperature for 30 min and concentrated. A solution of the residue in Et_2O (2 mL) was stirred at ambient tempareture for 15 min. The precipitate was collected by filtration, washed with Et_2O, and dried under reduced pressure to give *cis*-N^2-[4-(4-bromo-2-trifluoromethoxy-phenylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride (189 mg, 18%) as a white solid.

ESI MS m/e 524, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.04 (s, 1 H), 8.85 (d, J = 7.9 Hz, 1 H), 7.90 (d, J = 8.1 Hz, 1 H), 7.61-7.70 (m, 1 H), 7.53 (d, J = 7.6 Hz, 1 H), 7.22-7.31 (m, 1 H), 6.94 (s, 1 H), 6.79 (s, 1 H), 6.65 (s, 1 H), 4.28 (brs, 1H), 3.52 (s, 6 H), 3.30-3.45 (m, 2 H), 1.64-2.08 (m, 8 H).

Example 58



cis-*N*-[4-(4-Methylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-trifluoromethoxy-benzamid hydrochloride

Step A: Synthesis of *cis*-[4-(4-methylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-carbamic acid benzyl ester.

Using the procedure for the step G of Example 1, the title compound was obtained. ESI MS m/e 420, M (free) + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20-7.59 (m, 8 H), 7.04 (ddd, J = 8.2, 6.8, 1.3 Hz, 1 H), 5.54-5.76 (m, 1 H), 5.10 (s, 2 H), 4.78-5.24 (m, 2 H), 4.18-4.36 (m, 1 H), 3.11 (d, J = 4.8 Hz, 3 H), 2.92-3.16 (m, 2 H), 1.06-1.94 (m, 9 H).

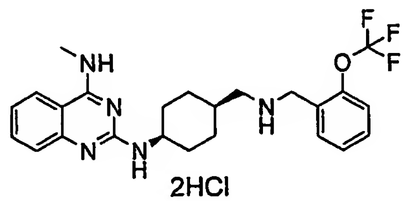
Step B: Synthesis of *cis*-*N*-[4-(4-methylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-trifluoromethoxy-benzamid hydrochloride.

To a solution of *cis*-[4-(4-methylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-carbamic acid benzyl ester (2.73 g, 6.50 mmol) in MeOH (27 mL) was added 10% Pd/C (273 mg). The mixture was stirred at 50 °C under hydrogen atmosphere for 14 hr, filtered, and concentrated to give a colorless solid (1.95 g). To a suspension of polymer supported DMAP (2.45 g, 7.35 mmol) in CH_2Cl_2 (10 mL) were added 2-trifluoromethoxy-benzoyl chloride (472 mg, 2.10 mmol) and the above solid (300 mg, 1.05 mmol). The mixture was stirred at ambient temperature for 2.5 days, filtered, poured into saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, purified by medium-pressure liquid chromatography (NH-silica gel, 50% EtOAc in hexane) and flash chromatography (silica gel, 20% MeOH in $CHCl_3$), and concentrated. To a solution of the residue in EtOAc (1 mL) was added 4 M hydrogen chloride in EtOAc (5 mL). The reaction mixture was stirred at ambient temperature for 30 min, and concentrated. A solution of the residue in Et_2O (5 mL) was stirred at ambient temperature for 1 hr and the precipitate was collected by filtration to give *cis*-*N*-[4-(4-methylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-trifluoromethoxy-benzamide hydrochloride (20 mg, 4%) as a white solid.

ESI MS m/e 474, M + H^+; ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.82 (s, 1 H), 8.63 (d, J = 7.3

Hz, 1 H), 7.97-8.12 (m, 2 H), 7.91 (dd, J = 7.6, 1.5 Hz, 1 H), 7.54 (t, J = 7.6 Hz, 1 H), 7.48 (dt, J = 7.9, 1.8 Hz, 1 H), 7.38 (t, J = 7.0 Hz, 1 H), 7.26-7.35 (m, 2 H), 7.19 (t, J = 7.6 Hz, 1 H), 6.77 (t, J = 5.8 Hz, 1 H), 4.30-4.41 (m, 1 H), 3.41 (t, J = 6.4 Hz, 2 H), 3.20 (d, J = 3.7 Hz, 3 H), 1.48-2.01 (m, 9 H).

Example 59



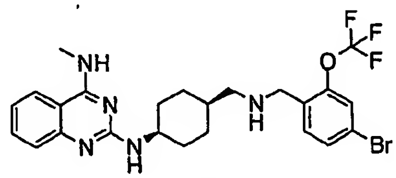
***cis*-N^4-Methyl-N^2-{4-[(2-trifluoromethoxy-benzylamino)-methyl]-cyclohexyl}-quinazoline-2,4-diamine dihydrochloride**

Step A: Synthesis of *cis*-N^4-methyl-N^2-{4-[(2-trifluoromethoxy-benzylamino)-methyl]-cyclohexyl}-quinazoline-2,4-diamine dihydrochloride.

To a solution of *cis*-[4-(4-methylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-carbamic acid benzyl ester obtained in step A of example 58 (2.73 g, 6.50 mmol) in MeOH (27 mL) was added 10% Pd/C (273 mg). The mixture was stirred at 50 °C under hydrogen atmosphere for 14 hr, filtered, and concentrated to give a colorless solid (1.95 g). To a solution of the above solid (300 mg, 1.05 mmol) in MeOH (3 mL) were added 2-trifluoromethoxy-benzaldehyde (200 mg, 1.05 mmol), AcOH (63 mg, 1.05 mmol), and $NaBH_3CN$ (99 mg, 1.58 mmol). The reaction mixture was stirred at ambient temperature with $CaCl_2$ tube for 4 hr, poured into 1 M aqueous sodium hydroxide, and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, purified by medium-pressure liquid chromatography (NH-silica gel, 50% EtOAc in hexane) and flash chromatography (silica gel, 10% MeOH in $CHCl_3$), and concentrated. To a solution of the residue in EtOAc (1 mL) was added 4 M hydrogen chloride in EtOAc (5 mL). The reaction mixture was stirred at ambient temperature for 30 min, and concentrated. A solution of the residue in Et_2O (10 mL) was stirred at ambient temperature for 1 hr and the precipitate was collected by filtration to give *cis*-N^4-methyl-N^2-{4-[(2-trifluoromethoxy-benzylamino)-methyl]-cyclohexyl}-quinazoline-2,4-diamine dihydrochloride (175 mg, 33%) as a white solid.

ESI MS m/e 460, M (free) + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.49 (brs, 1 H), 9.74 (brs, 1 H), 9.57 (d, J = 4.4 Hz, 1 H), 8.43 (d, J = 8.4 Hz, 1 H), 8.27 (d, J = 8.4 Hz, 1 H), 8.13 (dd, J = 7.5, 1.8 Hz, 1 H), 7.24-7.51 (m, 4 H), 6.95-7.16 (m, 2 H), 4.28 (s, 2 H), 4.13-4.38 (m, 1 H), 2.99 (d, J = 4.5 Hz, 3 H), 2.92 (d, J = 4.8 Hz, 2 H), 1.41-2.19 (m, 9 H).

Example 60



2HCl

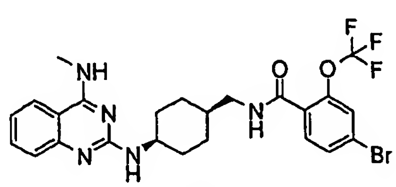
***cis*-*N*²-{4-[(4-Bromo-2-trifluoromethoxy-benzylamino)-methyl]-cyclohexyl}-*N*⁴-methyl-quinazoline-2,4-diamine dihydrochloride**

Step A: Synthesis of *cis*-*N*²-{4-[(4-bromo-2-trifluoromethoxy-benzylamino)-methyl]-cyclohexyl}-*N*⁴-methyl-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step A of Example 59, the title compound was obtained.

ESI MS m/e 538, M (free) + H^+; ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.23 (brs, 1 H), 9.75 (brs, 2 H), 9.46 (brs, 1 H), 8.43 (d, J = 7.9 Hz, 1 H), 8.29 (d, J = 8.5 Hz, 1 H), 8.08 (d, J = 8.5 Hz, 1 H), 7.55 (dd, J = 8.6, 1.8 Hz, 1 H), 7.44-7.52 (m, 2 H), 7.14 (t, J = 7.3 Hz, 1 H), 7.07 (d, J = 7.9 Hz, 1 H), 4.24 (s, 2 H), 4.19-4.30 (m, 1 H), 2.88-3.05 (m, 5 H), 1.38-1.84 (m, 9 H).

Example 61



HCl

cis-4-Bromo-N-[4-(4-methylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-trifluoromethoxy-benzamide hydrochloride

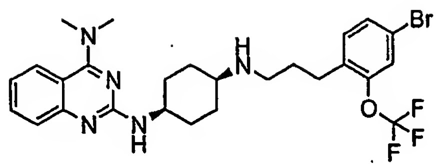
Step A: Synthesis of *cis*-4-bromo-*N*-[4-(4-methylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-trifluoromethoxy-benzamide hydrochloride.

To a solution of *cis*-[4-(4-Methylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-carbamic acid benzyl ester obtained in step A of example 58 (2.73 g, 6.50 mmol) in MeOH (27 mL) was sdded 10% Pd/C (273 mg). The mixture was stirred at 50 °C under hydrogen atmosphere for 14 hr, filtered, and concentrated to give *cis*-N^2-(4-Aminomethyl-cyclohexyl)-N^4-methyl-quinazoline-2,4-diamine (1.95 g) as a white solid. To a solution of 4-bromo-2-trifluoromethoxy-benzoic acid obtained in step B of example 13 (599 mg, 2.10 mmol) in CH_2Cl_2 (6 mL) was added DMF (1 μL, 14.7 μmol) and $SOCl_2$ (190 μL, 2.60 mmol). The mixture was stirred at reflux for 30 min and concentrated to give acid chloride as a pale yellow oil. To a suspension of polymer supported DMAP (2.45 g, 7.35 mmol) in CH_2Cl_2 (6 mL) were added above acid chloride and *cis*-N^2-(4-aminomethyl-cyclohexyl)-N^4-methyl-quinazoline-2,4-diamine (300 mg). The mixture was stirred at ambient temperature for 24 hr, filtered, poured into saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, purified by medium-pressure liquid chromatography (NH-silica gel, 50% EtOAc in hexane), and concentrated. To a solution of the residue in EtOAc (1 mL) was added 4 M hydrogen chloride in EtOAc (10 mL). The reaction mixture was stirred at ambient temperature for 1 hr, and concentrated. A solution of the residue in Et_2O (10 mL) was stirred at ambient temperature for 1 hr and the precipitate was collected by filtration to give *cis*-4-bromo-*N*-[4-(4-methylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-trifluoromethoxy-benzamide hydrochloride (47 mg, 8%) as a white solid.

ESI MS m/e 551, M (free)$^+$; ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.61 (s, 1 H), 8.56 (d, J = 7.3 Hz, 1 H), 8.40 (brs, 1 H), 8.15 (d, J = 8.5 Hz, 1 H), 7.78 (d, J = 8.5 Hz, 1 H), 7.47-7.55 (m, 2 H), 7.42 (t, J = 1.5 Hz, 1 H), 7.26 (d, J = 8.5 Hz, 1 H), 7.17 (t, J = 7.6 Hz, 1 H), 6.88 (t, J

= 5.8 Hz, 1 H), 4.32-4.44 (m, 1 H), 3.40 (t, J = 6.1 Hz, 2 H), 3.20 (d, J = 4.3 Hz, 3 H), 1.49-2. 00 (m, 8 H).

Example 62



2HCl

***cis*-N^2-{4-[3-(4-Bromo-2-trifluoromethoxy-phenyl)-propylamino] -cyclohexyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride**

Step A: Synthesis of (E)-3-(4-bromo-2-trifluoromethoxy-phenyl)-acrylic acid ethyl ester.

To a solution of (ethoxy-methoxymethyl-phosphinoyl)-acetic acid ethyl ester (3.45 g, 15.4 mmol) in THF (230 mL) was added 60% sodium hydride in oil (370 mg, 15.4 mmol). The mixture was stirred at ambient temperature for 50 min and cooled at 4 °C. To the reaction mixture was added 4-bromo-2-trifluoromethoxy-benzaldehyde (3 g, 11.2 mmol) in THF (100 mL). The mixture was stirred at ambient temperature for 15 hr. The solution was poured into H_2O, and the aqueous layer was extracted with EtOAc (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (silica gel, 5% EtOAc in hexane) to give (E)-3-(4-Bromo-2-trifluoromethoxy-phenyl)-acrylic acid ethyl ester (2.98 g, 79 %) as a colorless oil.

CI MS m/e 339, M + H^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.85 (d, J = 15.8 Hz, 1 H), 7.42-7.58 (m, 3 H), 6.48 (d, J = 15.8 Hz, 1 H), 4.29 (q, J = 7.0 Hz, 2 H), 1.35 (t, J = 7.0 Hz, 3 H).

Step B: Synthesis of 3-(4-bromo-2-trifluoromethoxy-phenyl)-propan-1-ol.

A suspension of lithium aluminum hydride (834 mg, 22.0 mmol) in Et_2O (20 mL) was cooled at 4 °C. A solution of (E)-3-(4-bromo-2-trifluoromethoxy-phenyl)-acrylic acid ethyl ester (2.98 g, 8.79 mmol) in Et_2O (9 mL) was added dropwise, and the mixture was

stirred at ambient temperature for 90 min. The reaction was quenched with EtOAc (6 mL) and saturated aqueous NH_4Cl was added dropwise. The aqueous layer was extracted with EtOAc (three times). The combined organic layer was washed with 1 M aqueous HCl, dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (silica gel, 25% EtOAc in hexane) to give 3-(4-bromo-2-trifluoromethoxy-phenyl)-propan-1-ol (1.14 g, 43 %) as a colorless oil.

EI MS m/e 298, M^+; ^1H NMR (300 MHz, $CDCl_3$) δ 7.10-7.43 (m, 3 H), 3.68 (t, J = 6.4 Hz, 2 H), 2.67-2.80 (m, 2 H), 1.75-1.94 (m, 2 H).

Step C: Synthesis of 3-(4-bromo-2-trifluoromethoxy-phenyl)-propionaldehyde.

A solution of 3-(4-bromo-2-trifluoromethoxy-phenyl)-propan-1-ol (1.03 g, 3.44 mmol) in CH_2Cl_2 (47 mL) was cooled at 4 °C and added celite (1.4 g) and pyridinium chlorochromate (1.11 g, 5.16 mmol). The reaction mixture was stirred at ambient temperature for 6 hr and filtered through a pad of celite, concentrated, and purified by flash chromatography (silica gel, 16% EtOAc in hexane) to give 3-(4-bromo-2-trifluoromethoxy-phenyl)-propionaldehyde (659 mg, 64%) as a colorless oil.

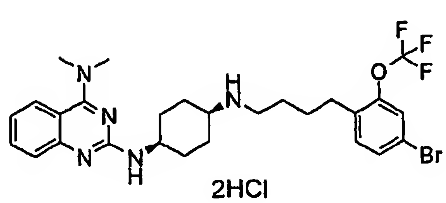
CI MS m/e 297, M + H^+; ^1H NMR (300 MHz, $CDCl_3$) δ 9.80 (t, J = 1.1 Hz, 1 H), 7.32-7.42 (m, 2 H), 7.17 (d, J = 8.4, Hz, 1 H), 2.96 (t, J = 7.4 Hz, 2 H), 2.72-2.81 (m, 2 H).

Step D: Synthesis of *cis*-N^2-{4-[3-(4-bromo-2-trifluoromethoxy-phenyl)-propylamino]-cyclohexyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step B of example 37, the title compound was obtained.

ESI MS m/e 566, M (free) + H^+; ^1H NMR (300 MHz, $CDCl_3$) δ 8.81 (d, J = 7.2 Hz, 1 H), 7.91 (d, J = 7.9 Hz, 1 H), 7.60-7.70 (m, 1 H), 7.49 (d, J = 8.4 Hz, 1 H), 7.12-7.42 (m, 5 H), 4.31 (brs, 1 H), 3.52 (s, 6 H), 3.23 (brs, 1 H), 3.02-3.14 (m, 2 H), 2.78 (t, J = 7.8 Hz, 2 H), 1.97-2.36 (m, 8 H), 1.59-1.85 (m, 2 H).

Example 63



cis-N^2-{4-[4-(4-Bromo-2-trifluoromethoxy-phenyl)-butylamino]-cyclohexyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride

Step A: Synthesis of (E)-4-(4-bromo-2-trifluoromethoxy-phenyl)-but-2-enoic acid ethyl ester.

Using the procedure for the step A of example 62, the title compound was obtained. ESI MS m/e 352, M^+; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33-7.53 (m, 3 H), 6.64 (d, J = 16.2 Hz, 1 H), 6.37 (dt, J = 16.0, 7.1 Hz, 1 H), 4.18 (q, J = 7.2 Hz, 2 H), 3.28 (dd, J = 7.1, 1.5 Hz, 2 H), 1.29 (t, J = 7.2 Hz, 3 H).

Step B: Synthesis of 4-(4-bromo-2-trifluoromethoxy-phenyl)-butan-1-ol.

Using the procedure for the step B of example 62, the title compound was obtained.

EI MS m/e 312, M^+; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.10-7.42 (m, 3 H), 3.68 (t, J = 5.1 Hz, 2 H), 2.60-2.82 (m, 2 H), 1.50-1.79 (m, 4 H), 1.10-1.50 (brs, 1 H).

Step C: Synthesis of 4-(4-bromo-2-trifluoromethoxy-phenyl)-butyraldehyde.

Using the procedure for the step C of example 62, the title compound was obtained.

ESI MS m/e 311, M + H^+; ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.79 (s, 1 H), 7.02-7.22 (m, 3 H), 2.60-2.84 (m, 2 H), 2.49 (t, J = 5.9 Hz, 2 H), 1.80-2.03 (m, 2 H).

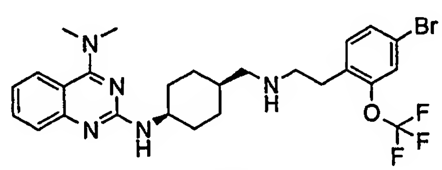
Step D: Synthesis of *cis*-N^2-{4-[4-(4-bromo-2-trifluoromethoxy-phenyl)-butylamino]-cyclohexyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride.

To a suspension of *cis*-N^2-(4-amino-cyclohexyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine obtained in step C of example 9 (240 mg, 0.84 mmol) in MeOH (3 mL) were added 4-(4-bromo-2-trifluoromethoxy-phenyl)-butyraldehyde (262 mg, 0.84 mmol), acetic acid (79 mg, 1.26 mmol), and $NaBH_3CN$ (79 mg, 1.26 mmol). The reaction mixture was

stirred at ambient temperature for 8 hr. The reaction was quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by medium-pressure liquid chromatography (NH-silica gel, 50% EtOAc in hexane) to give a pale yellow solid. To a solution of above solid in EtOAc (2 mL) was added 4 M hydrogen chloride in EtOAc (10 mL). The mixture was stirred at ambient temperature for 1 hr and concentrated. A solution of the residue in Et_2O (20 mL) was stirred at ambient tempareture for 1 hr. The solid was collected by filtration, washed with Et_2O, and dried under reduced pressure to give *cis*-N^2-{4-[4-(4-bromo-2-trifluoromethoxy-phenyl)-butylamino]-cyclohexyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride (220 mg, 40%) as a white solid.

ESI MS m/e 580, M (free) + H^+ ; ^1H NMR (200 MHz, $CDCl_3$) δ 12.73 (brs, 1 H), 9.55 (brs, 2 H), 8.66-8.88 (m, 1 H), 7.92 (d, J = 7.9 Hz, 1 H), 7.66 (t, J = 7.3 Hz, 1 H), 7.48 (d, J = 7.7 Hz, 1 H), 7.12-7.40 (m, 3 H), 4.20-4.42 (m, 1 H), 3.52 (s, 6 H), 2.92-3.42 (m, 3 H), 2.60-2.78 (m, 2 H), 1.58-2.59 (m, 12 H).

Example 64



2HCl

***cis*-N^2-(4-{[2-(4-Bromo-2-trifluoromethoxy-phenyl)-ethylamino]-methyl}-cyclohexyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride**

Step A: Synthesis of N^2-(4-aminomethyl-cyclohexyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine.

To a solution of *cis*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-carbamic acid benzyl ester obtained in step B of example 24 (12.1 g, 27.9 mmol) in MeOH (120 mL) was added 10% Pd/C (1.21 g). The mixture was stirred at 50 °C under hydrogen atmosphere for 19 hr, filtered, concentrated, and purified by flash

chromatography (NH-silica gel, 66% EtOAc in hexane to 15% MeOH in chloroform) to give N^2-(4-aminomethyl-cyclohexyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine (6.9 g, 83%) as a yellow solid.

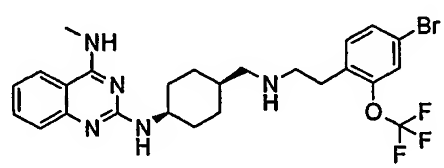
CI MS m/e 300, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 8.4 Hz, 1 H), 7.40-7.51 (m, 2 H), 6.98-7.04 (m, 1 H), 5.04 (d, J = 7.3 Hz, 1 H), 4.24-4.30 (m, 1 H), 3.27 (s, 6 H), 2.60 (d, J = 6.4 Hz, 2 H), 1.81-1.96 (m, 2 H), 1.57-1.76 (m, 4 H), 0.90-1.51 (m, 5 H).

Step B: Synthesis of *cis*-N^2-(4-{[2-(4-bromo-2-trifluoromethoxy-phenyl)-ethylamino]-methyl}-cyclohexyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step B of example 37, the title compound was obtained.

ESI MS m/e 566, M (free) + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.45 (s, 1 H), 9.74 (brs, 2 H), 8.70 (d, J = 7.6 Hz, 1 H), 7.90 (d, J = 8.4 Hz, 1 H), 7.66 (t, J = 7.6 Hz, 1 H), 7.17-7.52 (m, 4 H), 4.30 (brs, 1 H), 3.52 (s, 6 H), 3.32-3.50 (m, 2 H), 3.17 (brs, 2 H), 3.01 (brs, 2 H), 1.56-2.10 (m, 9 H).

Example 65



2HCl

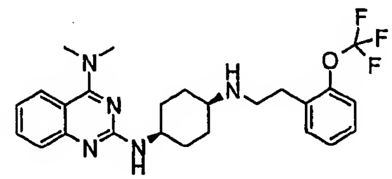
***cis*-N^2-(4-{[2-(4-Bromo-2-trifluoromethoxy-phenyl)-ethylamino]-methyl}-cyclohexyl)-N^4-methyl-quinazoline-2,4-diamine dihydrochloride**

Step A: Synthesis of *cis*-N^2-(4-{[2-(4-bromo-2-trifluoromethoxy-phenyl)-ethylamino]-methyl}-cyclohexyl)-N^4-methyl-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step A of example 59, the title compound was obtained.

ESI MS m/e 552 M (free) + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.66 (s, 1 H), 9.62 (brs, 1 H), 9.40 (brs, 1 H), 8.05-8.50 (m, 2 H), 7.21-7.58 (m, 4 H), 6.96-7.21 (m, 2 H), 4.26 (brs, 1 H), 3.41 (brs, 2 H), 2.75-3.31 (m, 7H), 1.30-2.24 (m, 9 H).

Example 66



2HCl

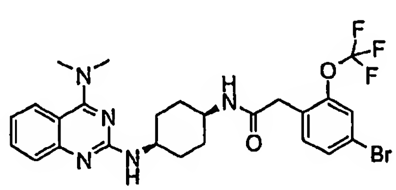
cis-N^4,N^4-Dimethyl-N^2-{4-[2-(2-trifluoromethoxy-phenyl)-ethylamino]-cyclohexyl}-quinazoline-2,4-diamine dihydrochloride

Step A: Synthesis of cis-N^4,N^4-dimethyl-N^2-{4-[2-(2-trifluoromethoxy-phenyl)-ethylamino]-cyclohexyl}-quinazoline-2,4-diamine dihydrochloride.

To a solution of *cis*-N^2-{4-[2-(4-bromo-2-trifluoromethoxy-phenyl)-ethylamino]-cyclohexyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride obtained in step B of example 37 (250 mg, 0.4 mmol) in EtOH (5 mL) was added 10% Pd/C (75 mg). The mixture was stirred at ambient temperature under hydrogen atmosphere for 17 hr, filtered, poured into saturated aqueous $NaHCO_3$. The aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica gel, 50% EtOAc in hexane) to give a colorless oil. To a solution of above oil in EtOAc (4 mL) was added 4 M hydrogen chloride in EtOAc (0.25 mL). The mixture was stirred at ambient temperature for 1 hr and concentrated. The residue was suspended with Et_2O (15 mL) and stirred at ambient tempareture for 1 hr. The solid was collected by filtration, washed with Et_2O, and dried under reduced pressure to give *cis*-N^4,N^4-dimethyl-N^2-{4-[2-(2-trifluoromethoxy-phenyl)-ethylamino]-cyclohexyl}-quinazoline-2,4-diamine dihydrochloride (104 mg, 48%) as a white solid.

ESI MS m/e 474, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.62 (s, 1 H), 9.78 (brs, 2 H), 8.71 (brs, 1 H), 7.93 (d, J = 8.4 Hz, 1 H), 7.39-7.77 (m, 3 H), 7.14-7.37 (m, 4 H), 4.33 (brs, 1 H), 3.15-3.71 (m, 11 H), 1.93-2.53 (m, 6 H), 1.62-1.89 (m, 2 H).

Example 67



HCl

***cis*-2-(4-Bromo-2-trifluoromethoxy-phenyl)-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-acetamide hydrochloride**

Step A: Synthesis of (4-bromo-2-trifluoromethoxy-phenyl)-acetic acid.

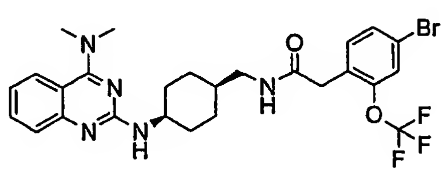
Using the procedure for the step B of example 13, the title compound was obtained.

ESI MS m/e 298, M^+ ; ^1H NMR (300 MHz, $CDCl_3$) δ 7.39-7.47 (m, 2 H), 7.22 (d, J = 8.1 Hz, 1 H), 3.70 (s, 2 H).

Step B: Synthesis of *cis*-2-(4-bromo-2-trifluoromethoxy-phenyl)-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-acetamide hydrochloride.

Using the procedure for the step A of example 47, the title compound was obtained.
ESI MS m/e 566, M (free) + H^+ ; ^1H NMR (300 MHz, $CDCl_3$) δ 13.15 (s, 1 H), 8.91 (d, J = 7.7 Hz, 1 H), 7.89 (d, J = 8.4 Hz, 1 H), 7.61-7.70 (m, 1 H), 7.48-7.56 (m, 1 H), 7.39-7.45 (m, 1 H), 7.21-7.33 (m, 2 H), 6.02 (d, J = 8.8 Hz, 1 H), 4.19-4.33 (m, 1 H), 3.82-4.03 (m, 1 H), 3.53 (s, 2 H), 3.51 (s, 6 H), 1.64-1.97 (m, 8 H).

Example 68



HCl

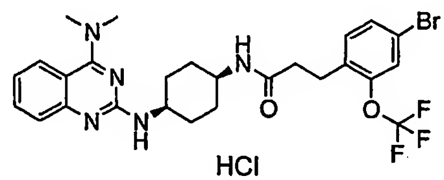
***cis*-2-(4-Bromo-2-trifluoromethoxy-phenyl)-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-acetamide hydrochloride**

Step A: Synthesis of *cis*-2-(4-bromo-2-trifluoromethoxy-phenyl)-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-acetamide hydrochloride.

Using the procedure for the step A of example 47, the title compound was obtained.

ESI MS m/e 580, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.85 (brs, 1 H), 9.08 (d, *J* = 8.4 Hz, 1 H), 7.90 (d, *J* = 8.8 Hz, 1 H), 7.58-7.72 (m, 1 H), 7.19-7.54 (m, 5 H), 6.81-6.98 (m, 1 H), 4.28-4.51 (m, 1 H), 3.83 (s, 2 H), 3.51 (s, 6 H), 3.29-3.34 (m, 2 H), 1.42-2.03 (m, 9 H).

Example 69



***cis*-3-(4-Bromo-2-trifluoromethoxy-phenyl)-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)cyclohexyl]-propionamide hydrochloride**

Step A: Synthesis of 3-(4-bromo-2-trifluoromethoxy-phenyl)-propionic acid.

To a solution of 3-(4-bromo-2-trifluoromethoxy-phenyl)-propan-1-ol obtained in step B of example 62 (1 g, 3.34 mmol) in acetone (15 mL) was added Jones reagent (4 mL) at 4 °C. The mixture was stirred at ambient temperature for 2 hr. The solution was poured into water (50 mL), and the aqueous layer was extracted with Et_2O (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (silica gel, 25% EtOAc in hexane) to give 3-(4-Bromo-2-trifluoromethoxy-phenyl)-propionic acid (930 mg, 89%) as a colorless oil.

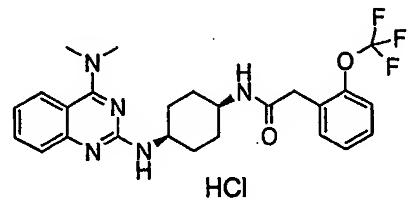
ESI MS m/e 313, M^+ ; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.31-7.50 (m, 2 H), 7.10-7.29 (m, 1 H), 2.97 (t, *J* = 7.7 Hz, 2 H), 2.65 (t, *J* = 7.7 Hz, 2 H).

Step B: Synthesis of *cis*-3-(4-bromo-2-trifluoromethoxy-phenyl)-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)cyclohexyl]-propionamide hydrochloride.

Using the procedure for the step A of example 47, the title compound was obtained.

ESI MS m/e 580, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.12 (brs, 1 H), 8.92 (d, *J* = 7.9 Hz, 1 H), 7.90 (d, *J* = 8.3 Hz, 1 H), 7.47-7.73 (m, 2 H), 7.15-7.44 (m, 3 H), 5.92 (d, *J* = 8.4 Hz, 1 H), 4.18-4.38 (m, 1 H), 3.76-4.03 (m, 1 H), 3.51 (s, 6 H), 2.98 (t, *J* = 7.7 Hz, 2 H), 2.44 (t, *J* = 7.7 Hz, 2 H), 1.55-1.96 (m, 9 H).

Example 70

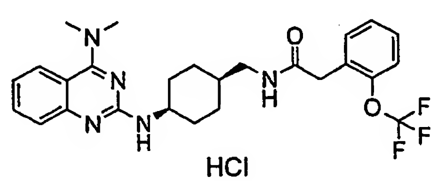


***cis-N*-[4-(4-Dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-2-(2-trifluoromethoxy-phenyl)-acetamide hydrochloride**

Step A: Synthesis of *cis-N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-2-(2-trifluoromethoxy-phenyl)-acetamide hydrochloride.

Using the procedure for the step A of example 47, the title compound was obtained. ESI MS m/e 488, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.20 (s, 1H), 8.84 (d, J = 7.6 Hz, 1 H), 7.89 (d, J = 8.7 Hz, 1 H), 7.60-7.70 (m, 1 H), 7.49-7.56 (m, 1 H), 7.20-7.43 (m, 5 H), 5.98 (d, J = 7.6 Hz, 1 H), 4.23 (brs, 1 H), 3.84-4.03 (m, 1 H), 3.59 (s, 2 H), 3.50 (s, 6 H), 1.62-1.98 (m, 8 H).

Example 71



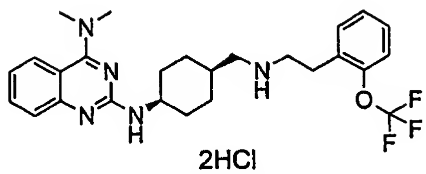
***cis-N*-[4-(4-Dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-(2-trifluoromethoxy-phenyl)-acetamide hydrochloride**

Step A: Synthesis of *cis-N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-(2-trifluoromethoxy-phenyl)-acetamide hydrochloride

Using the procedure for the step A of example 47, the title compound was obtained. ESI MS m/e 502, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.99 (s, 1 H), 8.99 (d, J = 8.5 Hz, 1 H), 7.90 (d, J = 8.2 Hz, 1 H), 7.63 (t, J = 7.62 Hz, 1 H), 7.38-7.54 (m, 2 H), 7.16-

7.34 (m, 4 H), 6.55 (brs, 1 H), 4.28-4.43 (m, 1 H), 3.81 (s, 2 H), 3.51 (s, 6 H), 3.27 (s, 2 H), 1.46-1.99 (m, 9 H).

Example 72



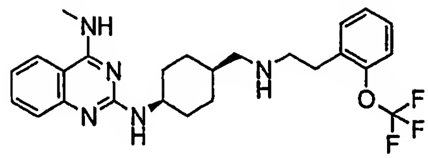
***cis*-N^4,N^4-Dimethyl-N^2-(4-{[2-(2-trifluoromethoxy-phenyl)-ethylamino]-methyl}-cyclohexyl)-quinazoline-2,4-diamine dihydrochloride**

Step A: *cis*-N^4,N^4-dimethyl-N^2-(4-{[2-(2-trifluoromethoxy-phenyl)-ethylamino]-methyl}-cyclohexyl)-quinazoline-2,4-diamine dihydrochloride

To a solution of *cis*-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-(2-trifluoromethoxy-phenyl)-acetamide (free) obtained in step A of example 71 (246 mg, 0.5 mmol) in THF (3.5 mL) was added 1 M borane-THF complex (2.45 mL, 2.45 mmol). The mixture was stirred at reflux for 2.5 h, and concentrated. To a solution of above residue in THF (3.5 mL) was added 1 M hydrochloric acid (4.41 mL, 4.41 mmol) . The mixture was stirred at reflux for 1 hr, and cooled to ambient temperature. To the reaction mixture was added 2 M aqueous sodium hydroxide, and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by medium-pressure liquid chromatography (NH-silica gel, 50% EtOAc in hexane) to give a colorless oil. To a solution of above oil in EtOAc (4 mL) was added 4 M hydrogen chloride in EtOAc (0.25 mL). The mixture was stirred at ambient temperature for 1 hr and concentrated. A solution of the residue in Et_2O (15 mL) was stirred at ambient temparetture for 1 hr. The precipitate was collected by filtration, washed with Et_2O, and dried under reduced pressure to give *cis*-N^4,N^4-dimethyl-N^2-{4-[2-(2-trifluoromethoxy-phenyl)-ethylamino]-cyclohexyl}-quinazoline-2,4-diamine dihydrochloride (81 mg, 30%) as a white solid.

FAB MS m/e 488, M + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.56 (s, 1 H), 9.72 (brs, 1 H), 8.72 (d, J = 7.7 Hz, 1 H), 7.90 (d, J = 8.2 Hz, 1 H), 7.66 (t, J = 7.7 Hz, 1 H), 7.42-7.54 (m, 2 H), 7.15-7.32 (m, 4 H), 4.22-4.35 (m, 1 H), 3.51 (s, 6 H), 3.38-3.59 (m, 2 H), 3.11-3.30 (m, 2 H), 2.92-3.07 (m, 2 H), 2.21 (brs, 1 H), 1.50-2.01 (m, 8 H).

Example 73



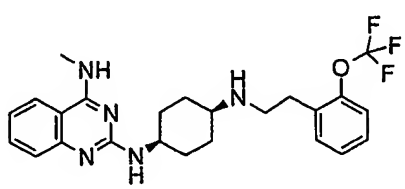
2HCl

***cis*-N^4-Methyl-N^2-(4-{[2-(2-trifluoromethoxy-phenyl)-ethylamino]-methyl}-cyclohexyl)-quinazoline-2,4-diamine dihydrochloride**

Step A: Synthesis of *cis*-N^4-methyl-N^2-(4-{[2-(2-trifluoromethoxy-phenyl)-ethylamino]-methyl}-cyclohexyl)-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step A of example 66, the title compound was obtained. ESI MS m/e 474, M (free) + H^+ ; ^{1}H NMR (200 MHz, $CDCl_3$) δ 11.72 (s, 1 H), 9.23-9.94 (m, 3 H), 8.00-8.66 (m, 2 H), 6.64-7.66 (m, 7 H), 4.26 (brs, 1 H), 2.73-3.65 (m, 9 H), 1.27-2.44 (m, 9 H).

Example 74



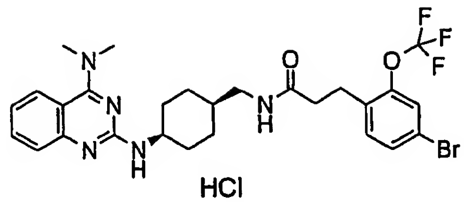
2HCl

***cis*-N^4-Methyl-N^2-{4-[2-(2-trifluoromethoxy-phenyl)-ethylamino]-cyclohexyl}-quinazoline-2,4-diamine dihydrochloride**

Step A: Synthesis of *cis*-N^4-methyl-N^2-{4-[2-(2-trifluoromethoxy-phenyl)-ethylamino]-cyclohexyl}-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step A of example 66, the title compound was obtained. ESI MS m/e 460, M (free) + H^+ ; ^{1}H NMR (200 MHz, $CDCl_3$) δ 12.20 (brs, 1 H), 9.84 (brs, 3 H), 8.59-8.79 (m, 1 H), 7.79-8.02 (m, 1 H), 7.10-7.70 (m, 7 H), 3.95-4.26 (m, 1 H), 3.09-3.54 (m, 5 H), 2.82-3.03 (m, 3 H), 1.57-2.43 (m, 8 H).

Example 75



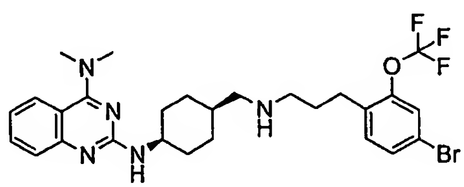
HCl

cis-3-(4-Bromo-2-trifluoromethoxy-phenyl)-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-propionamide hydrochloride

Step A: Synthesis of *cis*-3-(4-bromo-2-trifluoromethoxy-phenyl)-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-propionamide hydrochloride.

Using the procedure for the step A of example 47, the title compound was obtained. ESI MS m/e 594, M (free)$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.72 (s, 1 H), 9.01 (d, J = 8.7 Hz, 1 H), 7.90 (d, J = 8.2 Hz, 1 H), 7.65 (t, J = 7.6 Hz, 1 H), 7.47 (d, J = 7.6 Hz, 1 H), 7.21-7.41 (m, 3 H), 6.96 (brs, 1 H), 4.31-4.44 (m, 1 H), 3.51 (s, 6 H), 3.23-3.35 (m, 2 H), 3.03 (t, J = 7.6 Hz, 2 H), 2.76 (t, J = 7.6 Hz, 2 H), 1.38-1.98 (m, 9 H).

Example 76



2HCl

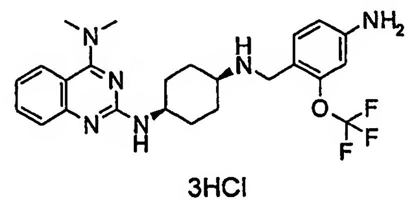
cis-N^2-(4-{[3-(4-Bromo-2-trifluoromethoxy-phenyl)-propylamino]-methyl}-cyclohexyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride

Step A: Synthesis of *cis*-N^2-(4-{[3-(4-bromo-2-trifluoromethoxy-phenyl)-propylamino]-methyl}-cyclohexyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step A of example 72, the title compound was obtained.

ESI MS m/e 580, M (free) + H^+ ; ^{1}H NMR (200 MHz, $CDCl_3$) δ 12.56 (s, 1 H), 9.40-9.71 (m, 2 H), 8.56-8.76 (m, 1 H), 7.91 (d, J = 8.4 Hz, 1 H), 7.66 (t, J = 7.6 Hz, 1 H), 7.13-7.47 (m, 5 H), 4.17-4.39 (m, 1 H), 3.51 (s, 6 H), 2.83-3.16 (m, 4 H), 2.67-2.82 (m, 2 H), 1.38-2.53 (m, 11 H).

Example 77



3HCl

***cis*-N^2-[4-(4-Amino-2-trifluoromethoxy-benzylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine trihydrochloride**

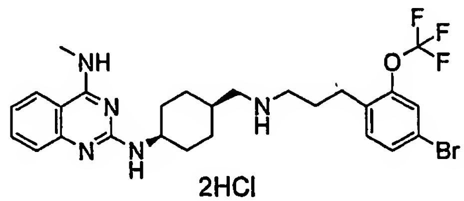
Step A: Synthesis of *cis*-N^2-[4-(4-amino-2-trifluoromethoxy-benzylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine trihydrochloride.

To a solution of *cis*-N^2-[4-(4-bromo-2-trifluoromethoxy-benzylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine obtained in step A of example 28 (1.5 g, 2.79 mmol) in EtOH (25 mL) were added copper powder (443 mg, 6.93 mmol), CuCl (690 mg, 2.79 mmol), and 28% aqueous NH_3 (25 mL). The reaction mixture was stirred at reflux for 3.5 hr. The mixture was poured into water, and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by medium-pressure liquid chromatography (NH-silica gel, 50% EtOAc in hexane) to give a colorless oil. To a solution of above oil in EtOAc (4 mL) was added 4 M hydrogen chloride in EtOAc (0.25 mL). The mixture was stirred at ambient temperature for 1 hr and concentrated. A solution of the residue in Et_2O (15 mL) was stirred at ambient tempareture for 1 hr. The precipitate was collected by filtration, washed with Et_2O, and dried under reduced pressure to give *cis*-N^2-[4-(4-amino-2-trifluoromethoxy-benzylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine trihydrochloride (104 mg, 6%) as a white solid.

ESI MS m/e 475, M (free) + H^+ ; ^{1}H NMR (300 MHz, DMSO-d_6) δ 13.08 (brs, 1 H), 9.15 (brs, 2 H), 8.32-8.48 (m, 1 H), 8.19 (d, J = 8.1 Hz, 1 H), 7.73-7.85 (m, 1 H), 7.46 (d, J =

8.4 Hz, 1 H), 7.37 (t, $J = 7.4$ Hz, 2 H), 6.56-6.71 (m, 2 H), 3.94-4.26 (m, 3 H), 3.49 (s, 6 H), 3.02-3.24 (m, 1 H), 1.59-2.09 (m, 8 H).

Example 78



***cis*-N^2-(4-{[3-(4-Bromo-2-trifluoromethoxy-phenyl)-propylamino]-methyl}-cyclohexyl)-N^4-methyl-quinazoline-2,4-diamine dihydrochloride**

Step A: Synthesis of N^2-(4-aminomethyl-cyclohexyl)-N^4-methyl-quinazoline-2,4-diamine

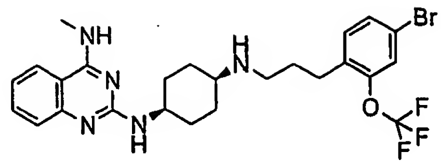
Using the procedure for the step A of example 64, the title compound was obtained. ESI MS m/e 286, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.59 (m, 3 H), 6.97-7.11 (m, 1 H), 5.59 (brs, 1 H), 5.00-5.18 (m, 1 H), 4.21-4.39 (m, 1 H), 3.13 (d, $J = 4.8$ Hz, 3 H), 2.61 (d, $J = 6.2$ Hz, 2 H), 1.57-1.99 (m, 5 H), 1.04-1.52 (m, 4 H).

Step B: Synthesis of *cis*-N^2-(4-{[3-(4-bromo-2-trifluoromethoxy-phenyl)-propylamino]-methyl}-cyclohexyl)-N^4-methyl-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step D of example 63, the title compound was obtained.

ESI MS m/e 566, M (free) + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.63 (s, 1 H), 9.45 (brs, 3 H), 8.41 (d, $J = 8.5$ Hz, 1 H), 8.32 (d, $J = 7.9$ Hz, 1 H), 7.46 (t, $J = 7.54$ Hz, 1 H), 7.24-7.39 (m, 3 H), 6.99-7.17 (m, 2 H), 4.13-4.35 (m, 1 H), 2.85-3.12 (m, 7 H), 2.75 (t, $J = 7.6$ Hz, 2 H), 2.27-2.47 (m, 2 H), 1.97-2.18 (m, 1 H), 1.37-1.91 (m, 8 H).

Example 79



2HCl

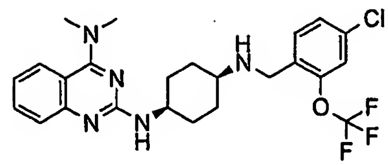
cis-N^2-{4-[3-(4-Bromo-2-trifluoromethoxy-phenyl)-propylamino]-cyclohexyl}-N^4-methyl-quinazoline-2,4-diamine dihydrochloride

Step A: Synthesis of cis-N^2-{4-[3-(4-bromo-2-trifluoromethoxy-phenyl)-propylamino]-cyclohexyl}-N^4-methyl-quinazoline-2,4-diamine dihydrochloride

To a suspension of *cis*-[4-(4-methylamino-quinazolin-2-ylamino)-cyclohexyl]-carbamic acid *tert*-butyl ester obtained in step B of example 50 (8.68 g, 23.4 mmol) in $CHCl_3$ (87mL) was added 4 M hydrogen chloride in EtOAc (100 mL). The reaction mixture was stirred at ambient temperature for 2 hr, and concentrated. The residue was alkalized with saturated aqueous $NaHCO_3$ and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated (10.57 g). To a suspension of the above residue (594 mg) in MeOH (6 mL) were added 3-(4-bromo-2-trifluoromethoxy-phenyl)-propionaldehyde obtained in step C of example 62 (650 mg, 2.19 mmol), AcOH (132 mg, 2.19 mmol), and $NaBH_3CN$ (207 mg, 3.29 mmol). The reaction mixture was stirred at ambient temperature for 16 hr, poured into saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, purified by medium-pressure liquid chromatography (NH-silica gel, 50% EtOAc in hexane and silica gel, 16% MeOH in $CHCl_3$) to give a yellow oil. To a solution of the residue in EtOAc (6 mL) was added 4 M hydrogen chloride in EtOAc (0.14 mL). The reaction mixture was stirred at ambient temperature for 30 min, and concentrated. A solution of the residue in Et_2O (10 mL) was stirred at ambient temperature for 1 hr and the precipitate was collected by filtration to give *cis*-N^2-{4-[3-(4-bromo-2-trifluoromethoxy-phenyl)-propylamino]-cyclohexyl}-N^4-methyl-quinazoline-2,4-diamine dihydrochloride (59 mg, 7%) as a white solid.

ESI MS m/e 552, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.37 (s, 1 H), 9.78 (brs, 1 H), 9.59 (brs, 2 H), 8.68 (d, J = 8.2 Hz, 1 H), 7.55-7.67 (m, 2 H), 7.27-7.43 (m, 5 H), 3.78-3.96 (m, 1 H), 2.94-3.24 (m, 3 H), 2.50-2.89 (m, 5 H), 2.09-2.50 (m, 6 H), 1.60-1.98 (m, 4 H).

Example 80



2HCl

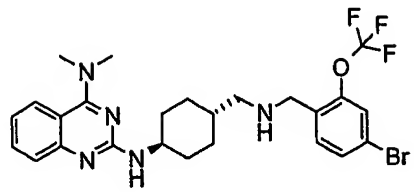
***cis*-N^2-[4-(4-Chloro-2-trifluoromethoxy-benzylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride**

Step A: Synthesis of *cis*-N^2-[4-(4-chloro-2-trifluoromethoxy-benzylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride.

A mixture of conc. HCl (420 μL) and $NaNO_2$ (44 mg, 0.64 mmol) were stirred at 70 °C for 10 min. To the reaction mixture was added a solution of *cis*-N^2-[4-(4-amino-2-trifluoromethoxy-benzylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine (free) obtained in step A of example 77 in AcOH (15 mL), and stirred at ambient temperature for 10 min. To the reaction mixture was added a solution of CuCl (146 mg, 1.47 mmol) in conc. HCl (1 mL), and stirred at 80 °C for 6 hr. The reaction mixture was alkalized with saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, purified by medium-pressure liquid chromatography (NH-silica gel, 50% EtOAc in hexane) to give a yellow oil. To a solution of above oil in EtOAc (2 mL) was added 4 M hydrogen chloride in EtOAc (10 mL). The mixture was stirred at ambient temperature for 1 hr and concentrated. A solution of the residue in Et_2O (20 mL) was stirred at ambient tempareture for 1 hr. The precipitate was collected by filtration, washed with Et_2O, and dried under reduced pressure to give *cis*-N^2-[4-(4-chloro-2-trifluoromethoxy-benzylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride (70 mg, 29%) as a white solid.

ESI MS m/e 494, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.66 (s, 1 H), 9.82-10.28 (m, 2 H), 8.78 (d, J = 7.6 Hz, 1 H), 8.24 (d, J = 8.3 Hz, 1 H), 7.92 (d, J = 8.2 Hz, 1 H), 7.67 (t, J = 7.6 Hz, 1 H), 7.47 (d, J = 8.1 Hz, 1 H), 7.18-7.41 (m, 3 H), 4.20-4.44 (m, 3 H), 3.52 (s, 6 H), 3.23 (brs, 1 H), 2.02-2.65 (m, 6 H), 1.75 (t, J = 12.8 Hz, 2 H).

Example 81



2HCl

***trans*-N^2-{4-[(4-Bromo-2-trifluoromethoxy-benzylamino)-methyl]-cyclohexyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride**

Step A: Synthesis of N^2-(4-aminomethyl-cyclohexyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine

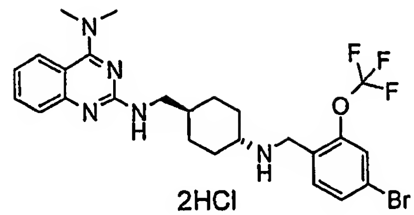
To a suspension of *trans*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-carbamic acid *tert*-butyl ester obtained in step B of example 6 (400 mg, 1.00 mmol) in EtOAc (10 mL) was added 4 M hydrogen chloride in EtOAc (5 mL). The mixture was stirred at ambient temperature for 80 min. The reaction mixture was alkalized with 2 M aqueous sodium hydroxide, and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, purified by medium-pressure liquid chromatography (NH-silica gel, 33% EtOAc in hexane to 3% MeOH in $CHCl_3$) to give N^2-(4-aminomethyl-cyclohexyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine (250 mg, 83%) as a pale yellow oil.

ESI MS m/e 300, M + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, J = 9.3 Hz, 1 H), 7.38-7.53 (m, 2 H), 6.97-7.05 (m, 1 H), 4.77 (d, J = 9.3 Hz, 1 H), 3.73-4.02 (m, 1 H), 3.26 (s, 6 H), 2.57 (d, J = 6.2 Hz, 2 H), 2.13-2.31 (m, 2 H), 1.75-1.96 (m, 2 H), 0.92-1.45 (m, 7 H).

Step B: Synthesis of *trans*-N^2-{4-[(4-bromo-2-trifluoromethoxy-benzylamino)-methyl]-cyclohexyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride

Using the procedure for the step B of example 37, the title compound was obtained ESI MS m/e 552, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.72 (s, 1 H), 10.19 (brs, 2 H), 8.18 (d, J = 8.9 Hz, 1 H), 8.06 (d, J = 7.9 Hz, 1 H), 7.91 (d, J = 8.3 Hz, 1 H), 7.42-7.65 (m, 3 H), 7.35 (d, J = 8.3 Hz, 1 H), 7.23 (t, J = 7.5 Hz, 1 H), 4.18-4.29 (m, 2 H), 3.69-3.89 (m, 1 H), 3.52 (s, 6 H), 2.64-2.81 (m, 2 H), 1.90-2.24 (m, 5 H), 1.02-1.56 (m, 4 H).

Example 82



***trans*-N^2-[4-(4-Bromo-2-trifluoromethoxy-benzylamino)-cyclohexylmethyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride**

Step A: Synthesis of *trans*-N^2-(4-amino-cyclohexylmethyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine.

To a solution of *trans*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexyl}-carbamic acid benzyl ester obtained in step C of example 3 (330 mg, 0.76 mmol) in MeOH (3.3 mL) was added 10% Pd/C (33 mg). The mixture was stirred at ambient temperature under hydrogen atmosphere for 25 hr, filtered, concentrated, and purified by flash chromatography (NH-silica gel, 50% EtOAc in hexane) to give *trans*-N^2-(4-amino-cyclohexylmethyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine (250 mg, 98%) as a pale yellow oil.

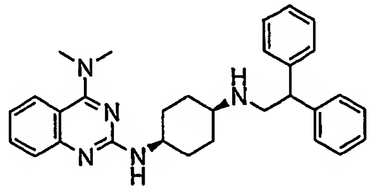
ESI MS m/e 300, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, J = 8.1 Hz, 1 H), 7.40-7.55 (m, 2 H), 6.95-7.07 (m, 1 H), 4.86-5.02 (m, 1 H), 3.36 (t, J = 6.3 Hz, 2 H), 3.26 (s, 6 H), 2.53-2.70 (m, 1 H), 1.77-1.98 (m, 4 H), 0.93-1.64 (m, 7 H).

Step B: Synthesis of *trans*-N^2-[4-(4-bromo-2-trifluoromethoxy-benzylamino)-cyclohexylmethyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride

Using the procedure for the step B of example 37, the title compound was obtained.

ESI MS m/e 552, M (free)$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.21 (s, 1 H), 10.03 (brs, 2 H), 8.34-8.47 (m, 1 H), 8.07 (d, J = 8.4 Hz, 1 H), 7.91 (d, J = 8.4 Hz, 1 H), 7.38-7.71 (m, 4 H), 7.20-7.34 (m, 1 H), 4.03-4.20 (m, 2 H), 3.51 (s, 6 H), 3.28-3.42 (m, 2 H), 2.65-2.92 (m, 1 H), 2.16-2.35 (m, 2 H), 1.86-2.05 (m, 2 H), 1.56-1.83 (m, 3 H), 0.89-1.16 (m, 2 H).

Example 83



2HCl

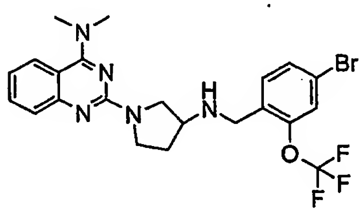
cis-N^2-[4-(2,2-Diphenyl-ethylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride

Step A: Synthesis of cis-N^2-[4-(2,2-diphenyl-ethylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride

Using the procedure for the step B of example 37, the title compound was obtained.

ESI MS m/e 466, M (free) + H^+ ; ^1H NMR (300 MHz, $CDCl_3$) δ 12.60 (brs, 1 H), 8.76-9.28 (m, 3 H), 7.91 (d, J = 8.3 Hz, 1 H), 7.59-7.71 (m, 2 H), 7.14-7.51 (m, 10 H), 5.00 (t, J = 7.7 Hz, 1 H), 4.30-4.40 (m, 1 H), 3.72 (d, J = 7.4 Hz, 2 H), 3.51 (s, 6 H), 3.19-3.43 (m, 1 H), 1.85-2.31 (m, 6 H), 1.52-1.76 (s, 2 H).

Example 84



2HCl

{2-[3-(4-Bromo-2-trifluoromethoxy-benzylamino)-pyrrolidin-1-yl]-quinazolin-4-yl}-dimethyl-amine dihydrochloride

Step A: Synthesis of [2-(3-amino-pyrrolidin-1-yl)-quinazolin-4-yl]-dimethyl-amine.

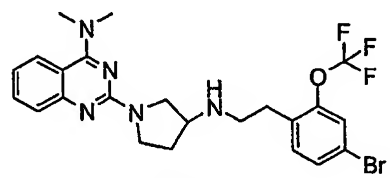
Using the procedure for the step A of example 81, the title compound was obtained. ESI MS m/e 258, M + H^+ ; ^1H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, J = 8.2 Hz, 1 H), 7.41-7.57 (m, 2 H), 6.93-7.06 (m, 1 H), 3.61-4.02 (m, 4 H), 3.40 (dd, J = 11.0, 4.97 Hz, 1 H), 3.26 (s, 6 H), 2.09-2.30 (m, 1 H), 1.68-1.87 (m, 1 H), 1.22-1.63 (m, 2 H).

Step B: Synthesis of {2-[3-(4-bromo-2-trifluoromethoxy-benzylamino)-pyrrolidin-1-yl]-quinazolin-4-yl}-dimethyl-amine dihydrochloride

Using the procedure for the step B of example 37, the title compound was obtained.

ESI MS m/e 510, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05-8.61 (m, 2 H), 7.61-7.96 (m, 2 H), 7.33-7.57 (m, 2 H), 7.17-7.31 (m, 1 H), 4.42-4.64 (m, 2 H), 4.34 (s, 2 H), 3.58-4.24 (m, 3 H), 3.46 (s, 6 H), 2.81 (brs, 1 H), 2.31-2.60 (m, 1 H).

Example 85



2HCl

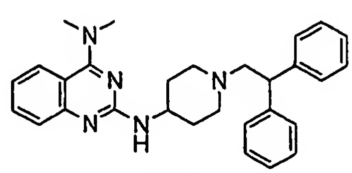
(2-{3-[2-(4-Bromo-2-trifluoromethoxy-phenyl)-ethylamino]-pyrrolidin-1-yl}-quinazolin-4-yl)-dimethyl-amine dihydrochloride

Step A: Synthesis of (2-{3-[2-(4-bromo-2-trifluoromethoxy-phenyl)-ethylamino]-pyrrolidin-1-yl}-quinazolin-4-yl)-dimethyl-amine dihydrochloride

Using the procedure for the step B of example 37, the title compound was obtained.

ESI MS m/e 524, M (free) H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15-8.53 (m, 1 H), 7.70-7.93 (m, 1 H), 7.62 (t, J = 7.6 Hz, 1 H), 7.11-7.46 (m, 4 H), 3.60-4.70 (m, 5 H), 3.45 (s, 6 H), 3.04-3.59 (m, 4 H), 2.29-2.98 (m, 2 H).

Example 86



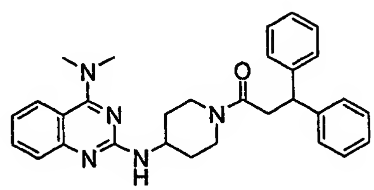
2HCl

N^2-[1-(2,2-Diphenyl-ethyl)-piperidin-4-yl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride

Step A: Synthesis of N^2-[1-(2,2-diphenyl-ethyl)-piperidin-4-yl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride

Using the procedure for the step B of example 37, the title compound was obtained ESI MS m/e 452, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.54 (brs, 1 H), 12.42 (s, 1 H), 9.82 (d, J = 8.4 Hz, 1 H), 7.92 (d, J = 8.1 Hz, 1 H), 7.66-7.74 (m, 1 H), 7.40-7.54 (m, 5 H), 7.27-7.39 (m, 5 H), 7.14-7.26 (m, 2 H), 5.17 (t, J = 6.3 Hz, 1 H), 4.39-4.56 (m, 1 H), 3.70-3.87 (m, 2 H), 3.34-3.60 (m, 7 H), 3.07-3.25 (m, 2 H), 2.55-2.87 (m, 2 H), 1.61-1.94 (m, 4 H).

Example 87



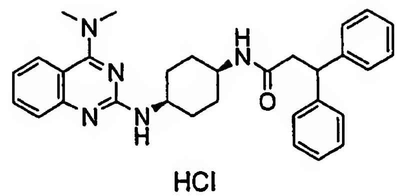
HCl

1-[4-(4-Dimethylamino-quinazolin-2-ylamino)-piperidin-1-yl]-3,3-diphenyl-propan-1-one hydrochloride

Step A: Synthesis of 1-[4-(4-dimethylamino-quinazolin-2-ylamino)-piperidin-1-yl]-3,3-diphenyl-propan-1-one hydrochloride

Using the procedure for the step A of example 47, the title compound was obtained. ESI MS m/e 502, M + Na^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.45 (brs, 1 H), 8.73 (d, J = 6.9 Hz, 1 H), 7.89 (d, J = 8.2 Hz, 1 H), 7.61-7.70 (m, 1 H), 7.56 (d, J = 7.6 Hz, 1 H), 7.25-7.39 (m, 11 H), 4.67 (t, J = 7.5 Hz, 1 H), 3.97-4.14 (m, 2 H), 3.70-3.89 (m, 1 H), 3.50 (s, 6 H), 3.13-3.30 (m, 2 H), 2.99-3.12 (m, 2 H), 1.31-1.99 (m, 4 H).

Example 88

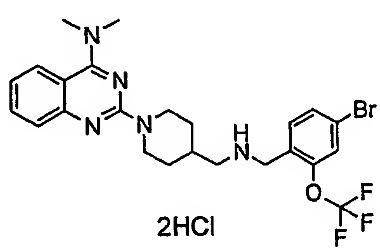


cis-N-[4-(4-Dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-3,3-diphenyl-propionamide hydrochloride

Step A: Synthesis of _cis-N_-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-3,3-diphenyl-propionamide hydrochloride

Using the procedure for the step A of example 47, the title compound was obtained. ESI MS m/e 494, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.20 (s, 1 H), 8.77 (d, J = 8.2 Hz, 1 H), 7.88 (d, J = 7.7 Hz, 1 H), 7.60-7.69 (m, 1 H), 7.53 (d, J = 17.1 Hz, 1 H), 7.12-7.33 (m, 11 H), 5.72 (d, J = 9.2 Hz, 1 H), 4.57 (t, J = 8.0 Hz, 1 H), 4.11-4.23 (m, 1 H), 3.72-3.87 (m, 1 H), 3.49 (s, 6 H), 2.88 (d, J = 7.9 Hz, 2 H), 1.47-1.85 (m, 8 H).

Example 89



(2-{4-[(4-Bromo-2-trifluoromethoxy-benzylamino)-methyl]-piperidin-1-yl}-quinazolin-4-yl)-dimethyl-amine dihydrochloride

Step A: Synthesis of [2-(4-aminomethyl-piperidin-1-yl)-quinazolin-4-yl]-dimethyl-amine.

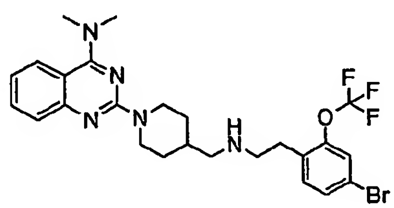
Using the procedure for the step A of example 64, the title compound was obtained. ESI MS m/e 286, M + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, J = 8.3 Hz, 1 H), 7.42-7.52 (m, 1 H), 7.23-7.36 (m, 1 H), 6.94-7.07 (m, 1 H), 4.94 (d, J = 12.7 Hz, 2 H), 3.26 (s, 6 H), 2.74-3.01 (m, 2 H), 2.61 (d, J = 6.6 Hz, 2 H), 1.46-1.99 (m, 4 H), 1.01-1.39 (m, 3 H).

Step B: Synthesis of (2-{4-[(4-bromo-2-trifluoromethoxy-benzylamino)-methyl]-piperidin-1-yl}-quinazolin-4-yl)-dimethyl-amine dihydrochloride.

Using the procedure for the step B of example 37, the title compound was obtained.

ESI MS m/e 538, M (free) +H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.66 (s, 1 H), 8.50 (d, J = 8.1 Hz, 1 H), 8.23 (d, J = 8.6 Hz, 1 H), 7.88 (d, J = 8.4 Hz, 1 H), 7.66 (t, J = 7.9 Hz, 1 H), 7.50 (dd, J = 8.4, 1.9 Hz, 1 H), 7.36-7.41 (m, 1 H), 7.24-7.34 (m, 1 H), 5.01 (brs, 2 H), 4.27 (s, 2 H), 3.49 (s, 6 H), 3.05-3.37 (m, 2 H), 2.44-2.92 (m, 3 H), 1.82-2.37 (m, 2 H), 1.14-1.62 (m, 2 H).

Example 90



2HCl

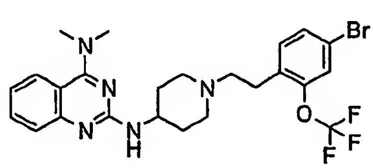
[2-(4-{[2-(4-Bromo-2-trifluoromethoxy-phenyl)-ethylamino]-methyl}-piperidin-1-yl)-quinazolin-4-yl]-dimethyl-amine dihydrochloride

Step A: Synthesis of [2-(4-{[2-(4-bromo-2-trifluoromethoxy-phenyl)-ethylamino]-methyl}-piperidin-1-yl)-quinazolin-4-yl]-dimethyl-amine dihydrochloride.

Using the procedure for the step B of example 37, the title compound was obtained.

ESI MS m/e 552, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.63 (s, 1 H), 8.48 (d, J = 8.2 Hz, 1 H), 7.79-7.97 (d, J = 7.5 Hz, 1 H), 7.58-7.73 (m, 1 H), 7.19-7.48 (m, 4 H), 5.02 (brs, 2 H), 3.49 (s, 6 H), 2.82-3.69 (m, 6 H), 1.98-2.79 (m, 5 H), 1.52 (brs, 2 H).

Example 91



2HCl

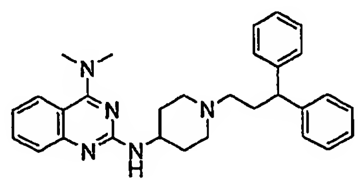
N^2-{1-[2-(4-Bromo-2-trifluoromethoxy-phenyl)-ethyl]-piperidin-4-yl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride

Step A: Synthesis of N^2-{1-[2-(4-bromo-2-trifluoromethoxy-phenyl)-ethyl]-piperidin-4-yl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step B of example 37, the title compound was obtained.

ESI MS m/e 538, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.61 (brs, 1 H), 12.43 (s, 1 H), 9.97 (d, J = 8.1 Hz, 1 H), 7.94 (d, J = 7.9 Hz, 1 H), 7.65-7.76 (m, 1 H), 7.28-7.52 (m, 5 H), 4.48-4.62 (m, 1 H), 3.12-3.73 (m, 14 H), 2.68-2.92 (m, 2 H), 1.96-2.13 (m, 2 H).

Example 92



2HCl

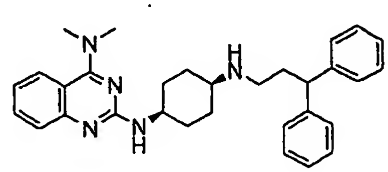
N^2-[1-(3,3-Diphenyl-propyl)-piperidin-4-yl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride

Step A: Synthesis of N^2-[1-(3,3-diphenyl-propyl)-piperidin-4-yl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step A of example 72, the title compound was obtained.

ESI MS m/e 466, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.42 (s, 1 H), 12.26 (brs, 1 H), 9.87 (d, J = 8.2 Hz, 1 H), 7.93 (d, J = 8.2 Hz, 1 H), 7.65-7.74 (m, 1 H), 7.47 (d, J = 8.2 Hz, 1 H), 7.13-7.37 (m, 11 H), 4.44-4.60 (m, 1 H), 3.98 (t, J = 7.9 Hz, 1 H), 3.28-3.65 (m, 10 H), 2.93-3.09 (m, 2 H), 2.63-2.88 (m, 4 H), 1.84-2.02 (m, 2 H).

Example 93



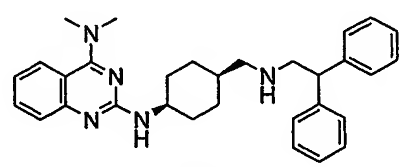
2HCl

***cis*-N^2-[4-(3,3-Diphenyl-propylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride**

Step A: Synthesis of *cis*-N^2-[4-(3,3-diphenyl-propylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step A of example 72, the title compound was obtained. ESI MS m/e 480, M (free) + H^+ ; ^1H NMR (300 MHz, $CDCl_3$) δ 12.58 (s, 1 H), 9.53 (s, 2 H), 8.58 (d, J = 7.9 Hz, 1 H), 7.91 (d, J = 8.1 Hz, 1 H), 7.64 (t, J = 7.7 Hz, 1 H), 7.48 (d, J = 7.9 Hz, 1 H), 7.08-7.33 (m, 11 H), 4.18-4.33 (m, 1 H), 4.11 (t, J = 7.7 Hz, 1 H), 3.50 (s, 6 H), 3.16 (brs, 1 H), 2.96 (brs, 2 H), 2.64-2.84 (m, 2 H), 1.87-2.25 (m, 6 H), 1.53-1.75 (m, 2 H).

Example 94



2HCl

***cis*-N^2-{4-[(2,2-Diphenyl-ethylamino)-methyl]-cyclohexyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride**

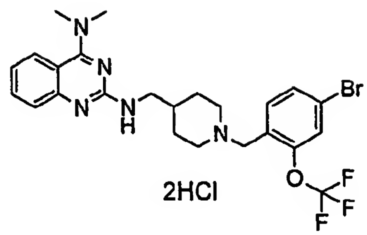
Step A: Synthesis of *cis*-N^2-{4-[(2,2-diphenyl-ethylamino)-methyl]-cyclohexyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride

Using the procedure for the step B of example 37, the title compound was obtained.

ESI MS m/e 480, M (free) + H^+ ; ^1H NMR (300 MHz, $CDCl_3$) δ 12.78 (s, 1 H), 8.94 (brs, 2 H), 8.80 (d, J = 8.4 Hz, 1 H), 7.89 (d, J = 8.1 Hz, 1 H), 7.60-7.69 (m, 1 H), 7.44-7.58 (m, 2 H), 7.18-7.42 (m, 9 H), 4.91 (t, J = 8.0 Hz, 1 H), 4.19-4.34 (m, 1 H), 3.61-3.76 (m, 2 H),

3.50 (s, 6 H), 2.81-2.97 (m, 2 H), 2.04-2.19 (m, 1 H), 1.74-1.91 (m, 2 H), 1.45-1.69 (m, 6 H).

Example 95



***N*²-[1-(4-Bromo-2-trifluoromethoxy-benzyl)-piperidin-4-ylmethyl]-*N*⁴,*N*⁴-dimethyl-quinazoline-2,4-diamine dihydrochloride**

Step A: Synthesis of *N*⁴,*N*⁴-dimethyl-*N*²-piperidin-4-ylmethyl-quinazoline-2,4-diamine.

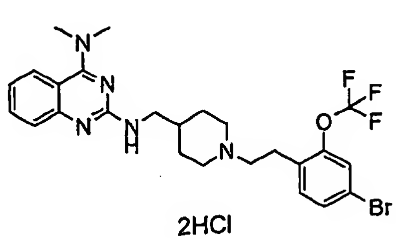
Using the procedure for the step A of example 81, the title compound was obtained. ESI MS m/e 408, M + Na^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, J = 8.3 Hz, 1 H), 7.39-7.59 (m, 2 H), 6.96-7.12 (m, 1 H), 4.79-5.11 (m, 1 H), 3.94-4.31 (m, 2 H), 3.42 (t, J = 5.9 Hz, 2 H), 3.27 (s, 6 H), 2.70 (t, J = 12.1 Hz, 2 H), 1.63-1.92 (m, 3 H), 1.46 (s, 9 H), 0.99-1.37 (m, 2 H).

Step B: Synthesis of *N*²-[1-(4-bromo-2-trifluoromethoxy-benzyl)-piperidin-4-ylmethyl]-*N*⁴,*N*⁴-dimethyl-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step B of example 37, the title compound was obtained.

ESI MS m/e 538, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.13 (s, 1 H), 12.69 (brs, 1 H), 8.73 (t, J = 6.3 Hz, 1 H), 8.19 (d, J = 8.2 Hz, 1 H), 7.90 (d, J = 7.6 Hz, 1 H), 7.45-7.73 (m, 4 H), 7.22-7.33 (m, 1 H), 4.10-4.24 (m, 2 H), 3.36-3.67 (m, 10 H), 2.61-2.86 (m, 2 H), 1.80-2.33 (m, 5 H).

Example 96



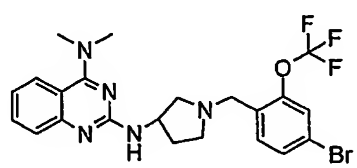
N^2-{1-[2-(4-Bromo-2-trifluoromethoxy-phenyl)-ethyl]-piperidin-4-ylmethyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride

Step A: Synthesis of N^2-{1-[2-(4-bromo-2-trifluoromethoxy-phenyl)-ethyl]-piperidin-4-ylmethyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride

Using the procedure for the step B of example 37, the title compound was obtained.

ESI MS m/e 552, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.16 (brs, 1 H), 8.74 (m, 1 H), 7.92 (d, J = 8.2 Hz, 1 H), 7.67 (t, J = 7.5 Hz, 1 H), 7.53 (d, J = 7.6 Hz, 1 H), 7.22-7.46 (m, 5 H), 3.44-3.71 (m, 10 H), 3.26-3.39 (m, 2 H), 3.01-3.15 (m, 2 H), 2.63-2.86 (m, 2 H), 1.87-2.33 (m, 5 H).

Example 97



2HCl

N^2-[1-(4-Bromo-2-trifluoromethoxy-benzyl)-pyrrolidin-3-yl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride

Step A: Synthesis of N^2-(1-benzyl-pyrrolidin-3-yl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine.

A mixture of (2-chloro-quinazolin-4-yl)-dimethyl-amine obtained in step B of example 1 (5.1 g, 28.9 mmol) and 1-Benzyl-pyrrolidin-3-ylamine (5.1 g, 28.9 mmol) in BuOH (8 mL) was stirred at reflux for 26 hr, poured into saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica gel, 10% to 16% EtOAc in hexane) to give N^2-(1-benzyl-pyrrolidin-3-yl)-N^4,N^4-dimethyl-

quinazoline-2,4-diamine (3.37 g, 50%) as a pale yellow solid.

ESI MS m/e 348, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, *J* = 9.0 Hz, 1 H), 7.46 (m, 2 H), 7.18-7.38 (m, 5 H), 7.02 (ddd, *J* = 8.3, 6.3, 1.9 Hz, 1 H), 5.30 (brs, 1 H), 4.59-4.75 (m, 1 H), 3.63 (d, *J* = 2.5 Hz, 2 H), 3.25 (s, 6 H), 2.88 (dd, *J* = 9.6, 6.6 Hz, 1 H), 2.70-2.81 (m, 1 H), 2.28-2.60 (m, 3 H), 1.64-1.78 (m, 1 H).

Step B: Synthesis of *N*^{4},*N*^{4}-dimethyl-*N*^{2}-pyrrolidin-3-yl-quinazoline-2,4-diamine.

To a solution of *N*^{2}-(1-benzyl-pyrrolidin-3-yl)-*N*^{4},*N*^{4}-dimethyl-quinazoline-2,4-diamine (3.3 g, 9.5 mmol) in MeOH (33 mL) was added $Pd(OH)_2$ (660 mg). The mixture was stirred at ambient temperature under hydrogen atmosphere for 13 hr, and stirred at 50 °C for 6 hr. The mixture was filtered, concentrated, and purified by medium-pressure liquid chromatography (NH-silica gel, 1% to 3% MeOH in $CHCl_3$) to give *N*^{4},*N*^{4}-dimethyl-*N*^{2}-pyrrolidin-3-yl-quinazoline-2,4-diamine (2.3 g, 93%) as a yellow oil.

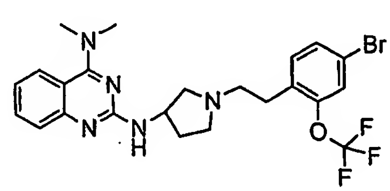
ESI MS m/e 258, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.8 Hz, 1 H), 7.42-7.54 (m, 2 H), 7.03 (ddd, *J* = 8.3, 6.4, 1.8 Hz, 1 H), 5.03 (brs, 1 H), 4.52 (brs, 1 H), 3.26 (s, 6 H), 2.83-3.24 (m, 4 H), 1.97-2.30 (m, 2 H), 1.57-1.77 (m, 1 H).

Step C: Synthesis of *N*^{2}-[1-(4-bromo-2-trifluoromethoxy-benzyl)-pyrrolidin-3-yl]-*N*^{4},*N*^{4}-dimethyl-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step B of example 37, the title compound was obtained.

ESI MS m/e 510, M (free) + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.22 (brs, 1 H), 12.87 (s, 1 H), 9.68 (d, *J* = 7.4 Hz, 1 H), 8.11 (d, *J* = 8.4 Hz, 1 H), 7.95 (d, *J* = 8.4 Hz, 1 H), 7.71 (t, *J* = 8.3 Hz, 1 H), 7.43-7.63 (m, 3 H), 7.28-7.38 (m, 1 H), 4.94-5.15 (m, 1 H), 4.41 (s, 2 H), 4.00-4.17 (m, 1 H), 3.26-3.82 (m, 8 H), 3.00-3.16 (m, 1 H), 2.59-2.82 (m, 1 H), 2.18-2.37 (m, 1 H).

Example 98



2HCl

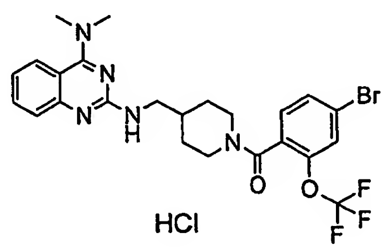
N^2-{1-[2-(4-Bromo-2-trifluoromethoxy-phenyl)-ethyl]-pyrrolidin-3-yl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride

Step A: Synthesis of N^2-{1-[2-(4-bromo-2-trifluoromethoxy-phenyl)-ethyl]-pyrrolidin-3-yl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step B of example 37, the title compound was obtained.

ESI MS m/e 524, M (free) + H^+ ; ^1H NMR (300 MHz, $CDCl_3$) δ 9.61-9.78 (m, 1 H), 7.96 (d, J = 8.4 Hz, 1 H), 7.71 (t, J = 7.7 Hz, 1 H), 7.55 (d, J = 8.2 Hz, 1 H), 7.29-7.47 (m, 4 H), 4.89-5.12 (m, 1 H), 4.07-4.28 (m, 1 H), 2.99-3.97 (m, 13 H), 2.55-2.79 (m, 1 H), 2.22-2.42 (m, 1 H).

Example 99

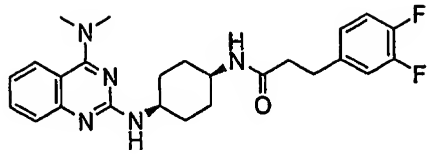


1-(4-Bromo-2-trifluoromethoxy-phenyl)-1-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-piperidin-1-yl}-methanone hydrochloride

Step A: Synthesis of 1-(4-bromo-2-trifluoromethoxy-phenyl)-1-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-piperidin-1-yl}-methanone hydrochloride.

Using the procedure for the step A of example 47, the title compound was obtained. ESI MS m/e 552, M (free) + H^+ ; ^1H NMR (300 MHz, $CDCl_3$) δ 13.44 (brs, 1 H), 8.53-8.77 (m, 1 H), 7.90 (d, J = 8.5 Hz, 1 H), 7.66 (t, J = 7.7 Hz, 1 H), 7.43-7.61 (m, 3 H), 7.19-7.37 (m, 1 H), 4.69-4.85 (m, 1 H), 3.20-3.63 (m, 10 H), 2.61-3.13 (m, 2 H), 1.76-2.14 (m, 3 H), 1.08-1.48 (m, 2 H).

Example 100



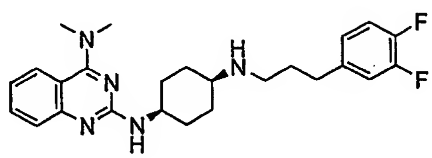
HCl

cis-3-(3,4-Difluoro-phenyl)-N-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-propionamide hydrochloride

Step A: Synthesis of cis-3-(3,4-difluoro-phenyl)-N-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-propionamide hydrochloride.

Using the procedure for the step A of example 47, the title compound was obtained. ESI MS m/e 454, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.05 (s, 1 H), 8.87 (d, J = 8.1 Hz, 1 H), 7.89 (d, J = 8.2 Hz, 1 H), 7.65 (t, J = 7.7 Hz, 1 H), 7.51 (d, J = 7.3 Hz, 1 H), 7.20-7.27 (m, 1 H), 6.88-7.09 (m, 3 H), 5.97 (d, J = 8.5 Hz, 1 H), 4.26 (brs, 1 H), 3.91 (brs, 1 H), 3.51 (s, 6 H), 2.92 (t, J = 7.6 Hz, 2 H), 2.44 (t, J = 7.6 Hz, 2 H), 1.61-1.93 (brs, 8 H).

Example 101



2HCl

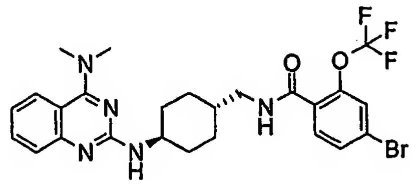
cis-N^2-{4-[3-(3,4-Difluoro-phenyl)-propylamino]-cyclohexyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride

Step A: Synthesis of cis-N^2-{4-[3-(3,4-difluoro-phenyl)-propylamino]-cyclohexyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step A of example 72, the title compound was obtained. ESI MS m/e 440, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.62 (s, 1 H), 9.54 (s, 2 H), 8.72 (d, J = 7.6 Hz, 1 H), 7.91 (d, J = 8.4 Hz, 1 H), 7.62-7.70 (m, 1 H), 7.48 (d, J = 7.6 Hz, 1 H), 7.24-7.33 (m, 1 H), 6.90-7.06 (m, 3 H), 4.29 (brs, 1 H), 3.52 (s, 6 H), 3.00-3.42

(m, 3 H), 2.67-2.81 (m, 2 H), 1.93-2.43 (m, 8 H), 1.60-1.80 (m, 2 H).

Example 102



HCl

***trans*-4-Bromo-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-trifluoromethoxy-benzamide hydrochloride**

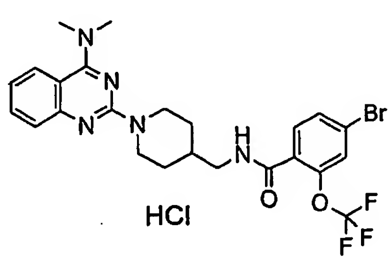
Step A: Synthesis of N^2-(4-aminomethyl-cyclohexyl)-N^4,N^4-dimethyl-quinazoline-2,4-diamine.

Using the procedure for the step A of example 81, the title compound was obtained. ESI MS m/e 300, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, J = 8.4 Hz, 1 H), 7.45 (m, 2 H), 7.00 (ddd, J = 8.4, 6.3, 1.9 Hz, 1 H), 4.80 (d, J = 8.2 Hz, 1 H), 3.82-3.94 (m, 1 H), 3.24 (s, 6 H), 2.56 (d, J = 6.2 Hz, 2 H), 2.14-2.28 (m, 2 H), 1.78-1.92 (m, 2 H), 0.95-1.42 (m, 7 H).

Step B: Synthesis of *trans*-4-bromo-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-2-trifluoromethoxy-benzamide hydrochloride.

Using the procedure for the step A of example 47, the title compound was obtained. ESI MS m/e 566, M + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.48 (s, 1 H), 8.34 (d, J = 7.5 Hz, 1 H), 7.83-7.94 (m, 2 H), 7.43-7.69 (m, 4 H), 7.20-7.29 (m, 1 H), 6.49-6.62 (m, 1 H), 3.72-3.93 (m, 1 H), 3.50 (s, 6 H), 3.39 (t, J = 6.3 Hz, 2 H), 2.09-2.22 (m, 2 H), 1.85-1.98 (m, 2 H), 1.37-1.69 (m, 3 H), 1.08-1.28 (m, 2 H).

Example 103

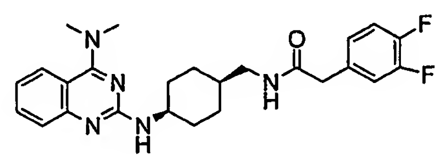


4-Bromo-*N*-[1-(4-dimethylamino-quinazolin-2-yl)-piperidin-4-ylmethyl]-2-trifluoromethoxy-benzamide hydrochloride

Step A: Synthesis of 4-bromo-*N*-[1-(4-dimethylamino-quinazolin-2-yl)-piperidin-4-ylmethyl]-2-trifluoromethoxy-benzamide hydrochloride.

Using the procedure for the step A of example 47, the title compound was obtained. ESI MS m/e 552, M (free)$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.50 (s, 1 H), 8.73 (d, J= 8.5 Hz, 1 H), 7.86 (d, J= 8.4 Hz, 1 H), 7.81 (d, J= 8.4 Hz, 1 H), 7.62-7.71 (m, 1 H), 7.53 (dd, J= 8.4, 1.87 Hz, 1 H), 7.45 (s, 1 H), 7.23-7.32 (m, 1 H), 6.77-6.87 (m, 1 H), 3.30-3.55 (m, 10 H), 2.96-3.27 (m, 2 H), 1.89-2.15 (m, 3 H), 1.28-1.57 (m, 2 H).

Example 104

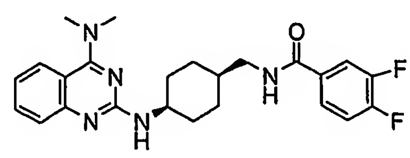


***cis*-2-(3,4-Difluoro-phenyl)-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-acetamide hydrochloride**

Step A: Synthesis of *cis*-2-(3,4-difluoro-phenyl)-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-acetamide hydrochloride

Using the procedure for the step A of example 47, the title compound was obtained. ESI MS m/e 454, M (free) + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.66 (s, 1 H), 9.08 (d, J= 8.9 Hz, 1 H), 7.90 (d, J= 8.1 Hz, 1 H), 7.66 (ddd, J= 8.4, 7.2, 1.2 Hz, 1 H), 7.48 (dd, J= 8.4, 0.9 Hz, 1 H), 7.32-7.41 (m, 1 H), 7.12-7.31 (m, 3 H), 6.97-7.08 (m, 1 H), 4.35-4.48 (m, 1 H), 3.78 (s, 2 H), 3.52 (s, 6 H), 3.28-3.36 (m, 2 H), 1.42-2.05 (m, 9 H).

Example 105

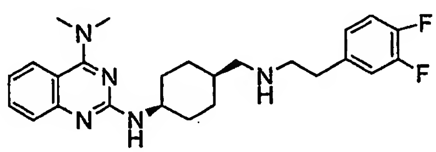


cis-N-[4-(4-Dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-3,4-difluoro-benzamide hydrochloride

Step A: Synthesis of _cis-N_-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-3,4-difluoro-benzamide hydrochloride.

Using the procedure for the step A of example 47, the title compound was obtained. ESI MS m/e 440, M (free) + H^+ ; ^1H NMR (300 MHz, $CDCl_3$) δ 12.89 (s, 1 H), 9.11 (d, J = 8.2 Hz, 1 H), 7.88 (m, 3 H), 7.64 (ddd, J = 8.4, 7.2, 1.2 Hz, 1 H), 7.49 (dd, J = 8.4, 0.9 Hz, 1 H), 7.18-7.29 (m, 2 H), 6.96-7.07 (m, 1 H), 4.29-4.44 (m, 1 H), 3.51 (s, 8 H), 1.55-2.02 (m, 9 H).

Example 106



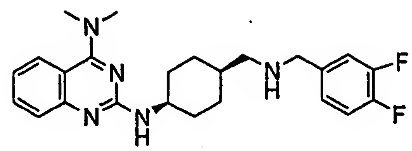
2HCl

cis-N²-(4-{[2-(3,4-Difluoro-phenyl)-ethylamino]-methyl}-cyclohexyl)-_N⁴,N⁴_-dimethyl-quinazoline-2,4-diamine dihydrochloride

Step A: Synthesis of _cis-N²_-(4-{[2-(3,4-difluoro-phenyl)-ethylamino]-methyl}-cyclohexyl)-_N⁴,N⁴_-dimethyl-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step A of example 72, the title compound was obtained. ESI MS m/e 440, M (free) + H^+ ; ^1H NMR (300 MHz, $CDCl_3$) δ 12.43 (s, 1 H), 9.64 (brs, 2 H), 8.66 (d, J = 8.3 Hz, 1 H), 7.91 (d, J = 8.3 Hz, 1 H), 7.67 (t, J = 7.8 Hz, 1 H), 7.46 (d, J = 8.3 Hz, 1 H), 7.28 (t, J = 7.8 Hz, 1 H), 6.97-7.17 (m, 3 H), 4.24-4.37 (m, 1 H), 3.52 (s, 6 H), 3.30-3.44 (m, 2 H), 2.94-3.25 (m, 4 H), 1.57-2.28 (m, 9 H).

Example 107



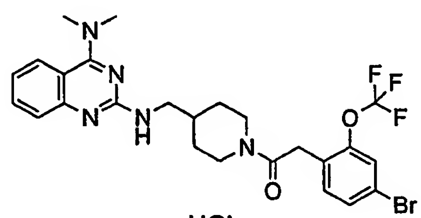
2HCl

cis-N^2-{4-[(3,4-Difluoro-benzylamino)-methyl]-cyclohexyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride

Step A: Synthesis of _cis_-N^2-{4-[(3,4-difluoro-benzylamino)-methyl]-cyclohexyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride

Using the procedure for the step A of example 72, the title compound was obtained. ESI MS m/e 426, M (free) + H^+ ; ^{1}H NMR (300 MHz, DMSO-d_6) δ 9.39 (s, 2 H), 8.44 (m, 1 H), 8.17 (d, J = 8.4 Hz, 1 H), 7.72-7.88 (m, 2 H), 7.27-7.61 (m, 4 H), 4.11-4.31 (m, 3 H), 3.48 (s, 6 H), 2.81 (d, J = 6.1 Hz, 2 H), 1.32-2.03 (m, 9 H).

Example 108



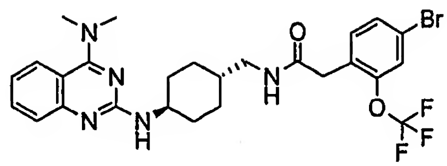
HCl

2-(4-Bromo-2-trifluoromethoxy-phenyl)-1-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-piperidin-1-yl}-ethanone hydrochloride

Step A: Synthesis of 2-(4-bromo-2-trifluoromethoxy-phenyl)-1-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-piperidin-1-yl}-ethanone hydrochloride.

Using the procedure for the step A of example 47, the title compound was obtained. ESI MS m/e 566, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.48 (s, 1 H), 8.65 (t, J = 5.8 Hz, 1 H), 7.90 (d, J = 8.4 Hz, 1 H), 7.53-7.70 (m, 2 H), 7.37-7.44 (m, 2 H), 7.20-7.32 (m, 2 H), 4.59-4.72 (m, 1 H), 3.80-3.94 (m, 1 H), 3.68 (d, J = 6.1 Hz, 2 H), 3.25-3.58 (m, 8 H), 2.94-3.12 (m, 1 H), 2.50-2.68 (m, 1 H), 1.75-2.03 (m, 3 H), 1.06-1.32 (m, 2 H).

Example 109



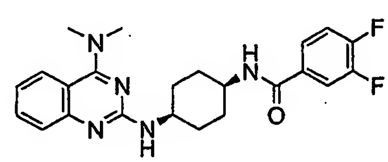
HCl

***trans*-2-(4-Bromo-2-trifluoromethoxy-phenyl)-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-acetamide**

Step A: Synthesis of *trans*-2-(4-bromo-2-trifluoromethoxy-phenyl)-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-acetamide.

Using the procedure for the step A of example 47, the title compound was obtained. ESI MS m/e 580, M (free)$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (d, J = 6.7 Hz, 1 H), 7.87-7.90 (d, J = 8.5 Hz, 1 H), 7.52-7.66 (m, 2 H), 7.39-7.44 (m, 2 H), 7.20-7.33 (m, 2 H), 5.85-5.98 (m, 1 H), 3.70-3.91 (m, 1 H), 3.58 (s, 2 H), 3.50 (s, 6 H), 3.16 (t, J = 6.5 Hz, 2 H), 2.03-2.20 (m, 2 H), 1.28-1.88 (m, 5 H), 0.96-1.18 (m, 2 H).

Example 110



HCl

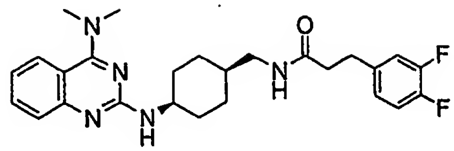
***cis*-*N*-[4-(4-Dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-3,4-difluoro-benzamide hydrochloride**

Step A: Synthesis of *cis*-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-3,4-difluoro-benzamide hydrochloride.

Using the procedure for the step A of example 47, the title compound was obtained. ESI MS m/e 448, M (free) + Na$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.01 (s, 1 H), 8.96 (d, J = 8.1 Hz, 1 H), 7.91 (d, J = 8.2 Hz, 1 H), 7.55-7.79 (m, 4 H), 7.49-7.54 (m, 1 H), 7.15-7.32 (m, 2 H), 6.76 (d, J = 8.4 Hz, 1 H), 4.30-4.41 (m, 1 H), 4.03-4.22 (m, 1 H), 3.52 (s, 6 H),

1.67-2.07 (m, 8 H).

Example 111



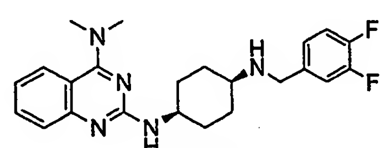
HCl

***cis*-3-(3,4-Difluoro-phenyl)-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-propionamide hydrochloride**

Step A: Synthesis of *cis*-3-(3,4-difluoro-phenyl)-*N*-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexylmethyl]-propionamide hydrochloride.

Using the procedure for the step A of example 47, the title compound was obtained. ESI MS m/e 468, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.70 (s, 1 H), 9.00 (d, J = 8.3 Hz, 1 H), 7.90 (d, J = 8.3 Hz, 1 H), 7.66 (ddd, J = 8.3, 7.2, 1.0 Hz, 1 H), 7.48 (dd, J = 8.3, 1.0 Hz, 1 H), 7.11-7.31 (m, 2 H), 6.84-7.06 (m, 3 H), 4.32-4.44 (m, 1 H), 3.51 (s, 6 H), 3.26-3.33 (m, 2 H), 2.96 (t, J = 7.5 Hz, 2 H), 2.76 (t, J = 7.4 Hz, 2 H), 1.34-1.94 (m, 9 H).

Example 112



2HCl

***cis*-N^2-[4-(3,4-Difluoro-benzylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride**

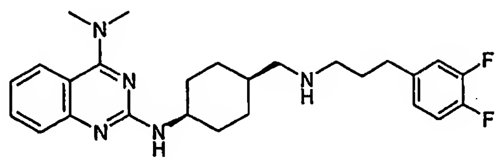
Step A: Synthesis of *cis*-N^2-[4-(3,4-difluoro-benzylamino)-cyclohexyl]-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step A of example 72, the title compound was obtained.

ESI MS m/e 434, M (free) + Na^+ ; ^{1}H NMR (300 MHz, DMSO-d_6) δ 13.03 (s, 1 H), 9.50

(brs, 2 H), 8.31-8.40 (m, 1 H), 8.19 (d, J = 8.2 Hz, 1 H), 7.73-7.90 (m, 2 H), 7.29-7.60 (m, 4 H), 4.04-4.28 (m, 3 H), 3.46 (s, 6 H), 3.06-3.22 (m, 1 H), 1.61-2.10 (m, 8 H).

Example 113



2HCl

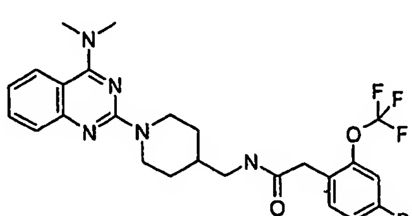
***cis-N²*-(4-{[3-(3,4-Difluoro-phenyl)-propylamino]-methyl}-cyclohexyl)-*N⁴,N⁴*-dimethyl-quinazoline-2,4-diamine dihydrochloride**

Step A: Synthesis of *cis-N²*-(4-{[3-(3,4-difluoro-phenyl)-propylamino]-methyl}-cyclohexyl)-*N⁴,N⁴*-dimethyl-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step A of example 72, the title compound was obtained.

ESI MS m/e 454, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.50 (s, 1 H), 9.43 (brs, 2 H), 8.60 (d, J = 7.93 Hz, 1 H), 7.90 (d, J = 8.2 Hz, 1 H), 7.65 (ddd, J = 8.2, 7.2, 1.1 Hz, 1 H), 7.46 (d, J = 8.6 Hz, 1 H), 7.23-7.30 (m, 1 H), 6.91-7.08 (m, 3 H), 4.22-4.34 (m, 1 H), 3.51 (s, 6 H), 2.87-3.07 (m, 4 H), 2.68 (t, J = 7.7 Hz, 2 H), 1.53-2.43 (m, 11 H).

Example 114



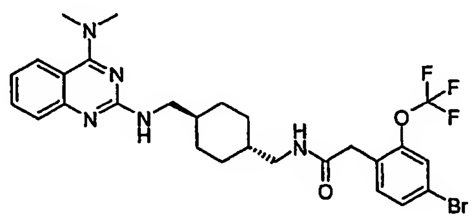
HCl

2-(4-Bromo-2-trifluoromethoxy-phenyl)-*N*-[1-(4-dimethylamino-quinazolin-2-yl)-piperidin-4-ylmethyl]-acetamide hydrochloride

Step A: Synthesis of 2-(4-bromo-2-trifluoromethoxy-phenyl)-*N*-[1-(4-dimethylamino-quinazolin-2-yl)-piperidin-4-ylmethyl]-acetamide hydrochloride

Using the procedure for the step A of example 47, the title compound was obtained. ESI MS m/e 588, M (free) + Na^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.32 (s, 1 H), 8.68 (d, *J* = 8.4 Hz, 1 H), 7.86 (d, *J* = 7.4 Hz, 1 H), 7.65 (ddd, *J* = 8.4, 7.1, 1.2 Hz, 1 H), 7.23-7.42 (m, 4 H), 6.59-6.69 (m, 1 H), 3.60 (s, 2 H), 3.48 (s, 7 H), 2.90-3.37 (m, 5 H), 1.78-2.08 (m, 3 H), 1.19-1.46 (m, 2 H).

Example 115



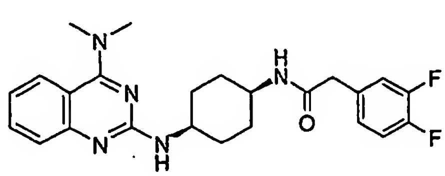
HCl

***trans*-2-(4-Bromo-2-trifluoromethoxy-phenyl)-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-acetamide hydrochloride**

StepA: Synthesis of *tarns*-2-(4-bromo-2-trifluoromethoxy-phenyl)-*N*-{4-[(4-dimethylamino-quinazolin-2-ylamino)-methyl]-cyclohexylmethyl}-acetamide hydrochloride.

Using the procedure for the step A of example 47, the title compound was obtained. ESI MS m/e 616, M (free) + Na^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.37-8.49 (m, 1 H), 7.89 (d, *J* = 8.5 Hz, 1 H), 7.53-7.68 (m, 2 H), 7.40-7.45 (m, 2 H), 7.20-7.32 (m, 2 H), 5.60-5.71 (m, 1 H), 3.55 (s, 2 H), 3.50 (s, 6 H), 3.35 (t, *J* = 6.1 Hz, 2 H), 3.08 (t, *J* = 6.4 Hz, 2 H), 0.77-2.00 (m, 10 H).

Example 116



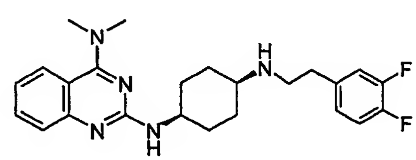
HCl

cis-2-(3,4-Difluoro-phenyl)-_N_-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-acetamide hydrochloride

Step A: Synthesis of _cis_-2-(3,4-difluoro-phenyl)-_N_-[4-(4-dimethylamino-quinazolin-2-ylamino)-cyclohexyl]-acetamide hydrochloride

Using the procedure for the step A of example 47, the title compound was obtained. ESI MS m/e 440, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 13.01 (s, 1 H), 8.85 (d, J = 8.2 Hz, 1 H), 7.89 (d, J = 8.2 Hz, 1 H), 7.65 (ddd, J = 8.2, 7.1, 1.2 Hz, 1 H), 7.52 (d, J = 8.2 Hz, 1 H), 6.95-7.33 (m, 4 H), 6.32 (d, J = 7.6 Hz, 1 H), 4.19-4.34 (m, 1 H), 3.82-4.01 (m, 1 H), 3.51 (s, 6 H), 3.47 (s, 2 H), 1.61-2.01 (m, 8 H).

Example 117



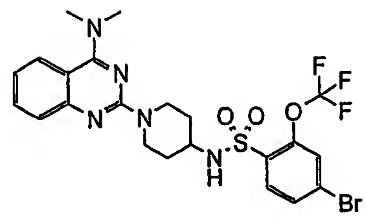
2HCl

cis-N^2-{4-[2-(3,4-Difluoro-phenyl)-ethylamino]-cyclohexyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride

Step A: Synthesis of _cis_-N^2-{4-[2-(3,4-difluoro-phenyl)-ethylamino]-cyclohexyl}-N^4,N^4-dimethyl-quinazoline-2,4-diamine dihydrochloride.

Using the procedure for the step A of example 72, the title compound was obtained. ESI MS m/e 426, M (free) + H^+ ; ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.51 (s, 1 H), 9.70 (brs, 2 H), 8.67 (d, J = 7.5 Hz, 1 H), 7.92 (d, J = 8.0 Hz, 1 H), 7.68 (t, J = 8.0 Hz, 1 H), 7.52 (d, J = 8.4 Hz, 1 H), 7.30 (t, J = 7.8 Hz, 1 H), 6.97-7.22 (m, 3 H), 4.34 (brs, 1 H), 3.53 (s, 6 H), 3.12-3.41 (m, 5 H), 1.62-2.40 (m, 8 H).

Example 118



4-Bromo-*N*-[1-(4-dimethylamino-quinazolin-2-yl)-piperidin-4-yl]-2-trifluoromethoxy-benzenesulfonamide

Step A: Synthesis of [2-(4-amino-piperidin-1-yl)-quinazolin-4-yl]-dimethyl-amine.

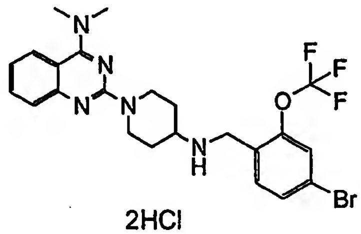
To a solution of 1-benzyl-piperidin-4-ylamine (2.00 g, 10.5 mmol) in THF (20 mL) was added $(Boc)_2O$ (2.52 g, 11.5 mmol) . The mixture was stirred at ambient temperature for 40 min, and concentrated. To a solution of the residue in MeOH (20 mL) was added 20% $Pd(OH)_2$ (400 mg). The mixture was stirred at ambient temperature under hydrogen atmosphere for 20 hr. Additionally, 20% $Pd(OH)_2$ (400 mg) was added and the mixture was stirred at ambient temperature under hydrogen atmosphere for 7 hr, at 50 °C for 4.5 hr, and at ambient temperature for 12 hr, filtered through a pad of celite, and concentrated to give a white solid. A mixture of (2-chloro-quinazolin-4-yl)-dimethyl-amine obtained in step B of example 1 (1.10 g, 5.30 mmol) and the above solid (1.27 g, 6.34 mmol) in 2-propanol (11 mL) was stirred at reflux for 20 hr. The precipitate was collected by filtration, washed with 2-propanol, dissolved in 50% MeOH in $CHCl_3$ (60 mL). The solution was poured into saturated aqueous $NaHCO_3$, and the aqueous layer was extracted with $CHCl_3$ (three times). The combined organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by flash chromatography (NH-silica gel, EtOAc to $CHCl_3$) to give [2-(4-amino-piperidin-1-yl)-quinazolin-4-yl]-dimethyl-amine (864 mg, 68%) as a colorless oil. ESI MS m/e 272, M + H^+ ; ^1H NMR (300 MHz, $CDCl_3$) δ 7.79 (d, J = 8.2 Hz, 1 H), 7.45-7.55 (m, 2 H), 6.96-7.05 (m, 1 H), 4.83 (d, J = 13.4 Hz, 2 H), 3.26 (s, 6H), 2.84-3.03 (m, 3 H), 1.85-1.95 (m, 2 H), 1.20-1.50 (m, 4 H).

Step B: Synthesis of 4-bromo-*N*-[1-(4-dimethylamino-quinazolin-2-yl)-piperidin-4-yl]-2-trifluoromethoxy-benzenesulfonamide.

Using the procedure for the step A of example 20, the title compound was obtained.

ESI MS m/e 574, M +H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.94 (d, J = 8.7 Hz, 1 H), 7.80 (d, J = 8.2 Hz, 1 H), 7.39-7.61 (m, 4 H), 6.98-7.07 (m, 1 H), 4.60-4.81 (m, 3 H), 3.39-3.61 (m, 1 H), 3.25 (s, 6 H), 2.98-3.08 (m, 2 H), 1.73-1.92 (m, 2 H), 1.33-1.54 (m, 2 H).

Example 119



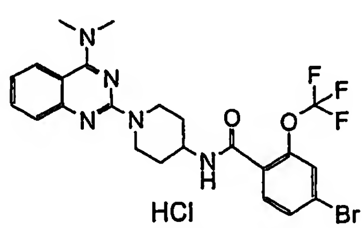
{2-[4-(4-Bromo-2-trifluoromethoxy-benzylamino)-piperidin-1-yl]-quinazolin-4-yl}-dimethyl-amine dihydrochloride

Step A: Synthesis of {2-[4-(4-bromo-2-trifluoromethoxy-benzylamino)-piperidin-1-yl]-quinazolin-4-yl}-dimethyl-amine dihydrochloride.

Using the procedure for the step B of example 37, the title compound was obtained.

ESI MS m/e 524, M (free) + H$^+$; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.43 (d, J = 8.1 Hz, 1 H), 8.20 (d, J = 8.4 Hz, 1 H), 7.90 (d, J = 8.4 Hz, 1 H), 7.67 (t, J = 7.5 Hz, 1 H), 7.26-7.49 (m, 3 H), 5.13 (brs, 2 H), 4.27 (s, 2 H), 3.08-3.60 (s, 9 H), 2.08-2.78 (m, 4 H).

Example 120

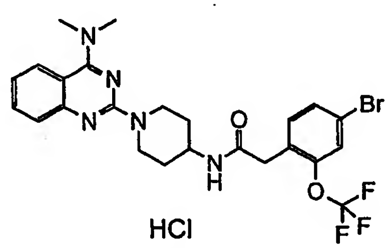


4-Bromo-*N*-[1-(4-dimethylamino-quinazolin-2-yl)-piperidin-4-yl]-2-trifluoromethoxy-benzamide hydrochloride

Step A: Synthesis of 4-bromo-*N*-[1-(4-dimethylamino-quinazolin-2-yl)-piperidin-4-yl]-2-trifluoromethoxy-benzamide hydrochloride.

Using the procedure for the step A of example 47, the title compound was obtained. ESI MS m/e 560, M (free) Na^+ ; ^1H NMR (300 MHz, $CDCl_3$) δ 13.68 (s, 1 H), 8.73 (d, *J* = 7.8 Hz, 1 H), 7.80-7.91 (m, 2 H), 7.68 (ddd, *J* = 8.4, 7.1, 1.3 Hz, 1 H), 7.55 (dd, *J* = 8.4, 1.9 Hz, 1 H), 7.42-7.46 (m, 1 H), 7.29 (ddd, *J* = 8.4, 7.1, 1.3 Hz, 1 H), 6.67 (d, *J* = 7.3 Hz, 1 H), 5.04 (brs, 2 H), 4.23-4.42 (m, 1 H), 3.27-3.61 (m, 8 H), 2.19-2.36 (m, 2 H), 1.57-1.81 (m, 2 H).

Example 121



2-(4-Bromo-2-trifluoromethoxy-phenyl)-*N*-[1-(4-dimethylamino-quinazolin-2-yl)-piperidin-4-yl]-acetamide hydrochloride

Step A: Synthesis of 2-(4-bromo-2-trifluoromethoxy-phenyl)-*N*-[1-(4-dimethylamino-quinazolin-2-yl)-piperidin-4-yl]-acetamide hydrochloride.

Using the procedure for the step A of example 47, the title compound was obtained. ESI MS m/e 574, M (free) + Na^+ ; ^1H NMR (300 MHz, $CDCl_3$) δ 13.08 (s, 1 H), 8.61 (d, *J* = 8.4 Hz, 1 H), 7.86 (d, *J* = 7.5 Hz, 1 H), 7.56-7.68 (m, 2 H), 7.21-7.39 (m, 4 H), 4.70-5.10 (m, 2 H), 4.04-4.22 (m, 1 H), 3.68 (s, 2 H), 3.34-3.61 (m, 8 H), 1.59-2.19 (m, 4 H).

Example 122 - 301.

To a solution of amine obtained in step A of example 15 (30 μmol) and pyridine (120 μmol) in CH_2Cl_2 (400 μL) was added an appropriate sulfonyl chloride (60 μmol) in

CH_2Cl_2 (200 μL) at 25 °C. After stirring at the same temperature for 20 hr, the reaction mixture was concentrated by a stream of dry N_2. To the residue was partitionated between $CHCl_3$ and saturated aqueous NH_4Cl. The aqueous layer was extracted with $CHCl_3$. The combined organic layers were dried over $MgSO_4$. After concentration by a stream of dry N_2, dry CH_2Cl_2 (600 μL) and PSA (300 μL) were added to the residue. After the stirring at 25 °C for 20 hr, the reaction mixture was filtrated and purified by flash chromatography (NH-silica gel, 33% MeOH in $CHCl_3$) to give the desired product.

Example 302 - 588.

To a solution of amine obtained in step C of example 9 or step A of example 64 (30 μmol) in CH_2Cl_2 (200 μL) were added poly(4-vinylpyridine) (75 μL) in CH_2Cl_2 (200 μL) and acid chloride (60 μmol) in CH_2Cl_2 (200 μL) at 25 °C. After stirring at the same temperature for 20 hr, the reaction mixture was filtered and concentrated by a stream of dry N_2. To the residue were added dry CH_2Cl_2 (600 μL) and PSA (300 μL). After the stirring at 25 °C for 20 hr, the reaction mixture was filtrated and purified by flash chromatography (NH-silica gel, 33% MeOH in $CHCl_3$) to give the desired product.

Example 589 - 1136.

To a solution of carboxylic acid (200 μL, 60 μmol) in CH_2Cl_2 (200 μL) were added 1-cyclohexyl-3-methylpolystyrene-carbodiimide (150 μL, 126 μmol) in CH_2Cl_2 (200 μL) and amine obtained in step C of example 9 or step A of example 64 (30 μmol) in CH_2Cl_2 (200 μL) at 25 °C. After stirring at the same temperature for 20 hr, the reaction mixture was filtered through NH-silica gel, and concentrated by a stream of dry N_2. To the residue were added dry CH_2Cl_2 (700 μL) and polystyrene linked benzaldehyde (75 μL, 60 μmol). After the stirring at 50 °C for 20 hr, the reaction mixture was filtrated, and concentrated by a stream of dry N_2 to give the desired product.

Example 1137 - 1745.

To a solution of the amide product in THF (200 μl) was added 1 M borane-THF

complex in THF (300 μl, 300 μmol). The mixture was stirred at 80 °C for 1 hr, and concentrated by a stream of dry N_2. To the residue were added 1 M aqueous HCl (300 μl) and THF (300 μl). The mixture was stirred at 80 °C for 1 hr, and concentrated by a stream of dry N_2. To the residue was partitionated between $CHCl_3$ and 2 M aqueous sodium hydroxide. The aqueous layer was extracted with $CHCl_3$. The combined organic layers were dried over $MgSO_4$. The mixture was concentrated by a stream of dry N_2, and the purified by flash chromatography (silica gel, 2% to 7% 2 M NH_3/MeOH in $CHCl_3$) to give the desired product.

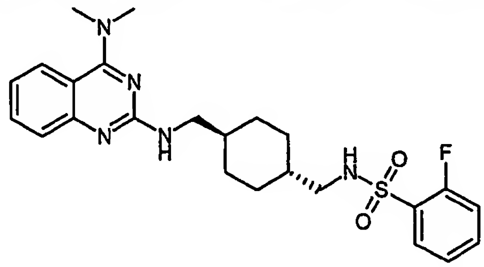
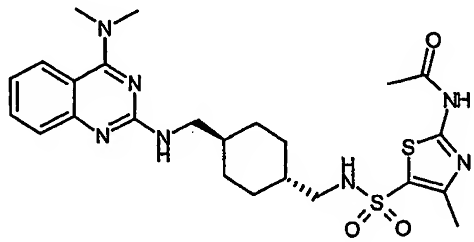
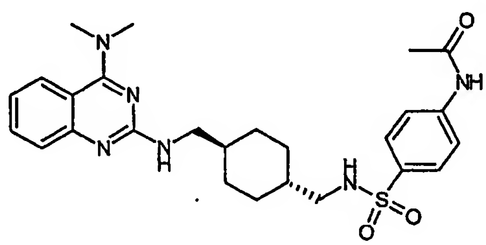
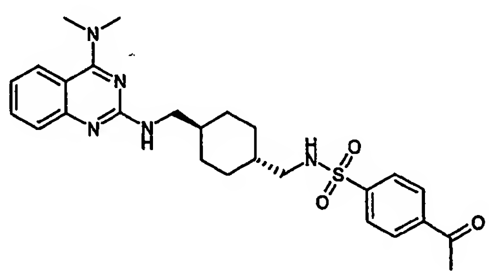
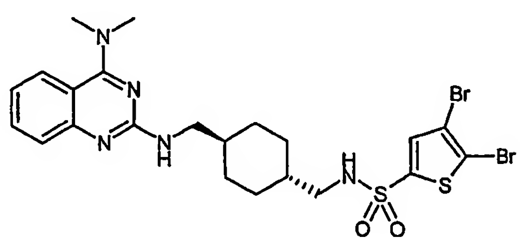
Example 1746 - 2184.

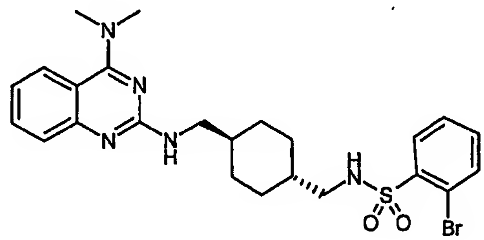
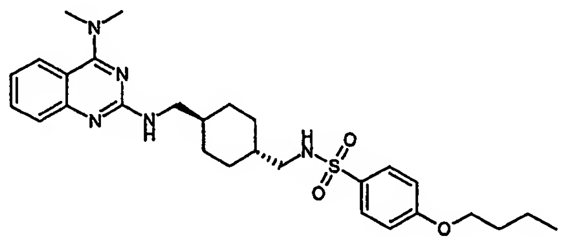
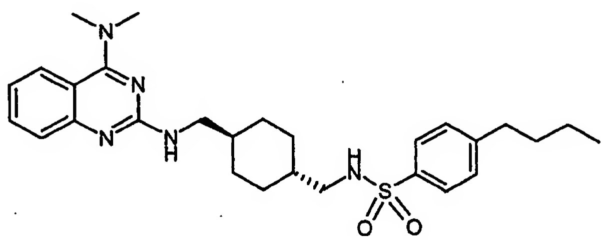
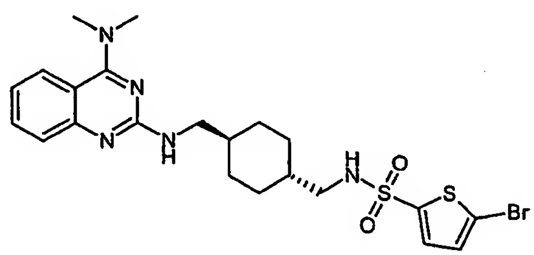
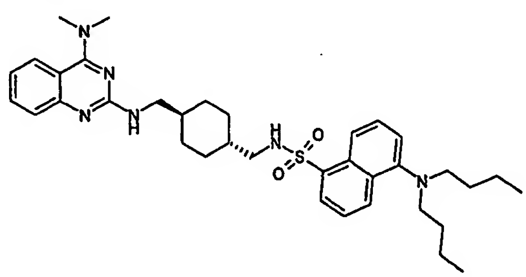
To a solution of amine obtained in step C of example 9 or step A of example 64 (36 μmol) in MeOH (200 μL) were added aldehyde (30 μmol) in MeOH (200 μL) and AcOH (90 μmol) at 25 °C. The reaction mixture was stirred at the same temperature for 1 hr. To the mixture was added $NaBH_3CN$ (120 μmol) in MeOH (200 μL). After stirring at the same temperature for 20 hr, the reaction mixture was concentrated by a stream of dry N_2. To the residue was partitionated between $CHCl_3$ and 2 M aqueous sodium hydroxide. The aqueous layer was extracted with $CHCl_3$. The combined organic layers were dried over $MgSO_4$. The mixture was concentrated by a stream of dry N_2, and purified by flash chromatography (silica gel, 2% to 7% 2 M NH_3/MeOH in $CHCl_3$) to give the desired product.

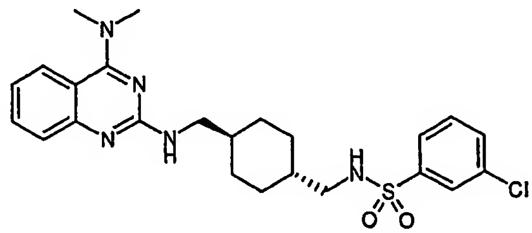
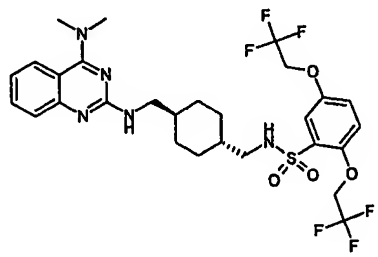
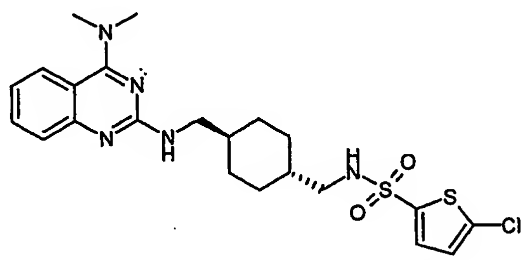
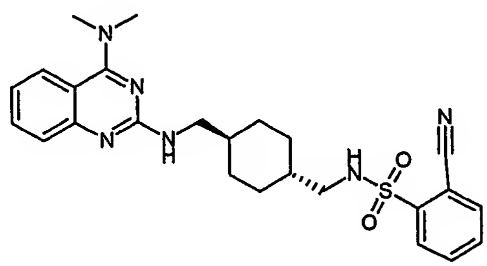
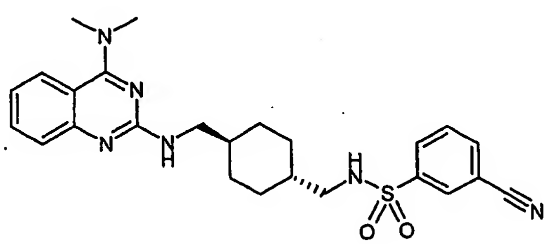
Example 2185 - 2328.

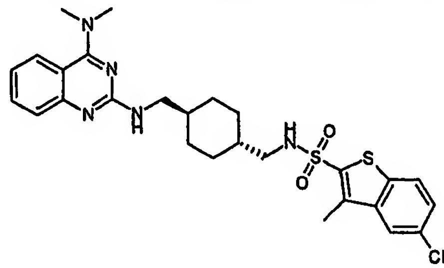
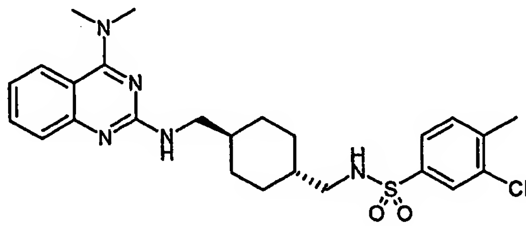
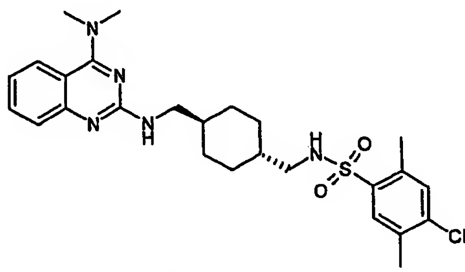
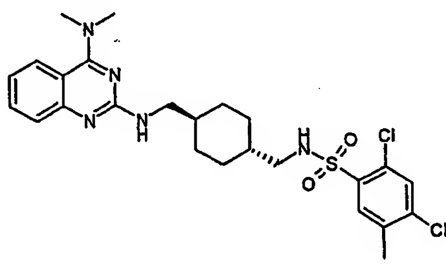
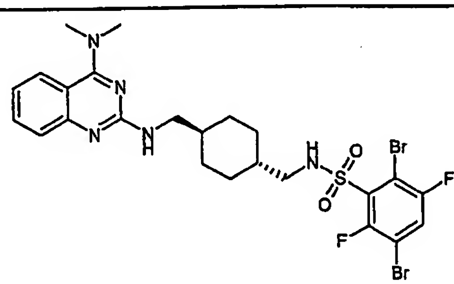
To a solution of alcohol (35 μmol) in CH_2Cl_2 (200 μL) was added Dess-Martin periodinane (63 μmol) in CH_2Cl_2 (200 μL) at 25 °C, and the reaction mixture was stirred at the same temperature for 20 hr. To the reaction mixture were added amine obtained in step C of example 9 or step A of example 64 (36 μmol) in MeOH (200 μL) and AcOH (90 μL), and the mixture was stirred at the same temperature for 1 hr. To the mixture was added $NaBH_3CN$ (120 μmol) in MeOH (200 μL). After stirring at the same temperature for 20 hr, the reaction mixture was concentrated by a stream of dry N_2. To the residue was partitionated between $CHCl_3$ and 2 M aqueous sodium hydroxide. The aqueous layer was

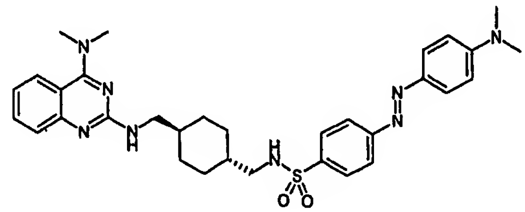
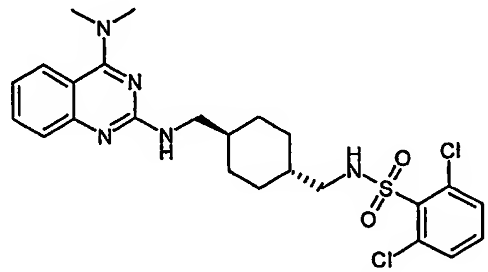
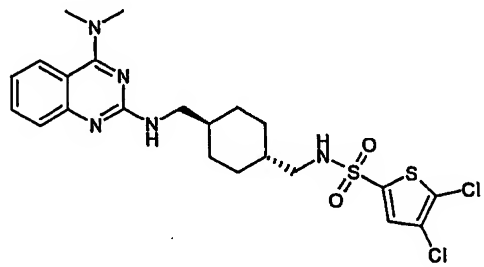
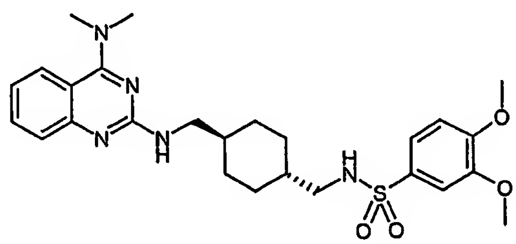
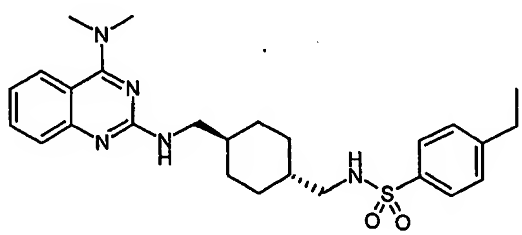
extracted with $CHCl_3$. The combined organic layers were dried over $MgSO_4$. The mixture was concentrated by a stream of dry N_2, and purified by flash chromatography (silica gel, 2% to 7% 2 M NH_3/MeOH in $CHCl_3$) to give the desired product.

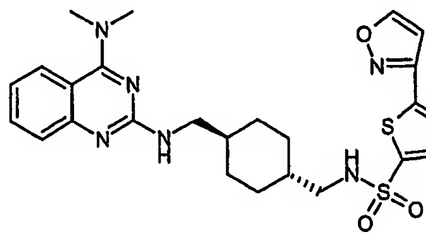
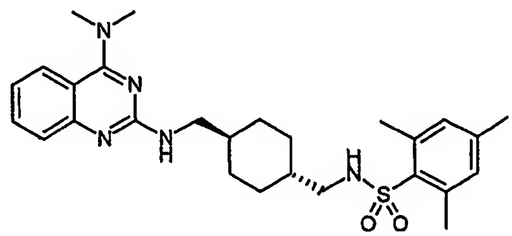
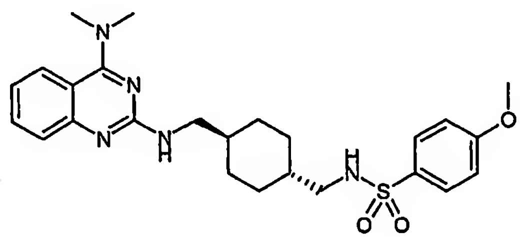
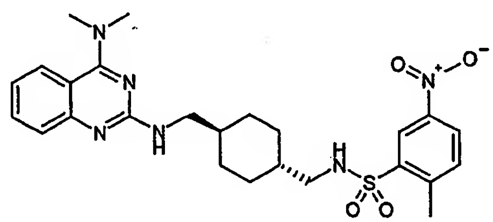
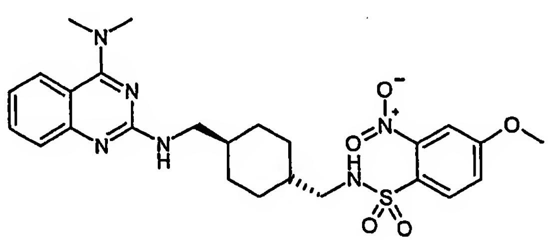
Example No.	Structure	APCI-MS
122		472 (M + H)
123		532 (M + H)
124		511 (M + H)
125		496 (M + H)
126		616 (M + H)

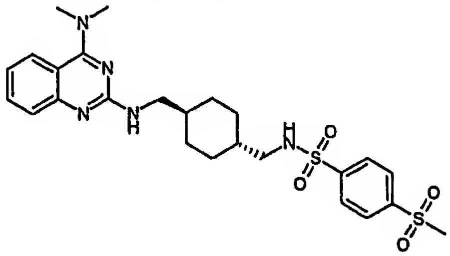
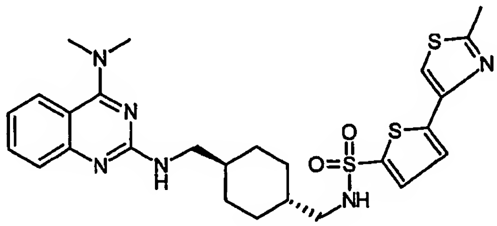
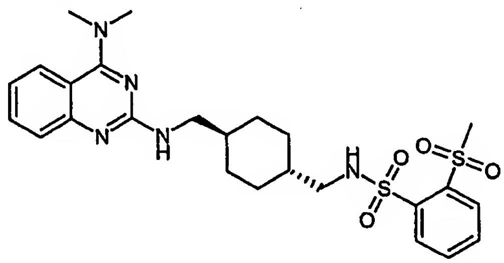
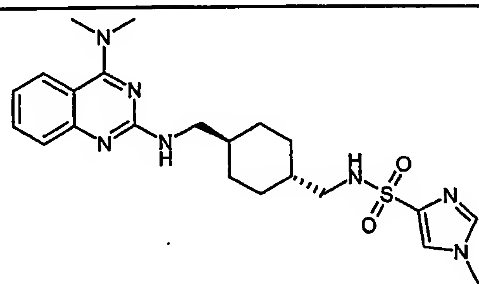
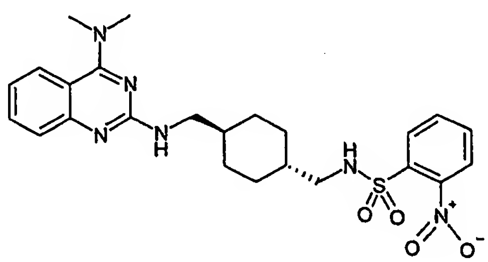
Example No.	Structure	APCI-MS
127		532 (M + H)
128		526 (M + H)
129		510 (M + H)
130		538 (M + H)
131		631 (M + H)

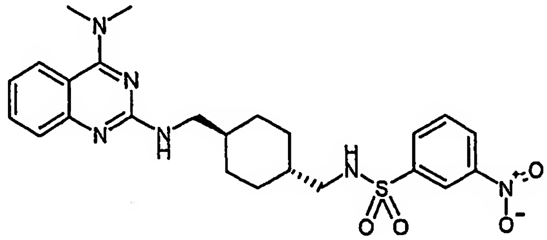
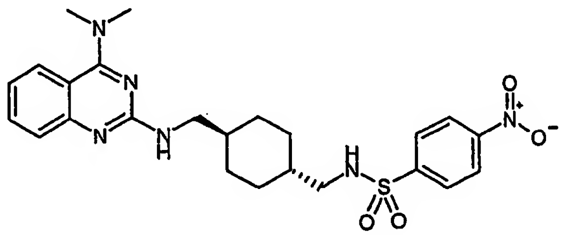
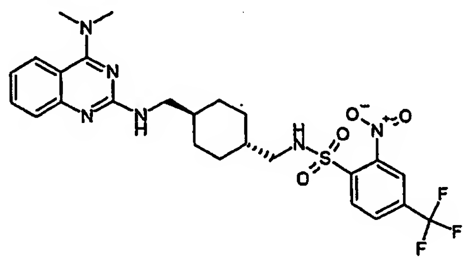
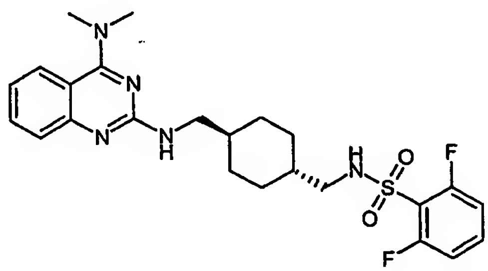
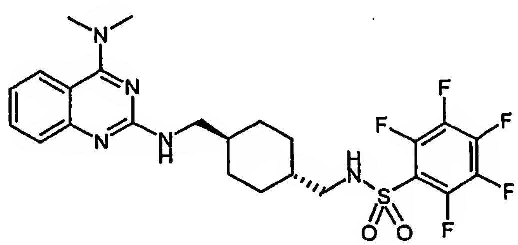
Example No.	Structure	APCI-MS
132		488 (M + H)
133		650 (M + H)
134		494 (M + H)
135		479 (M + H)
136		479 (M + H)

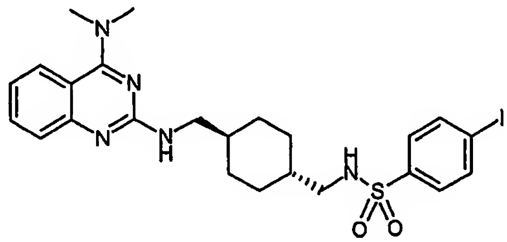
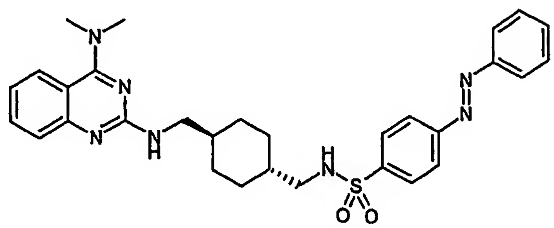
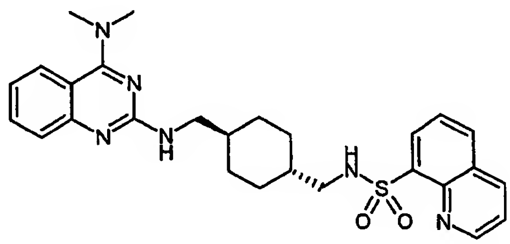
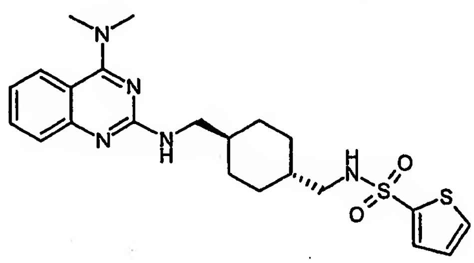
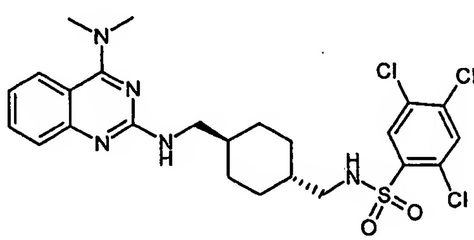
Example No.	Structure	APCI-MS
137		558 (M + H)
138		502 (M + H)
139		516 (M + H)
140		536 (M + H)
141		646 (M + H)

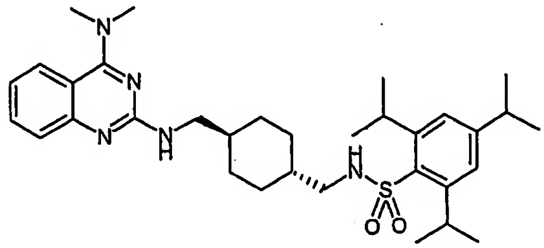
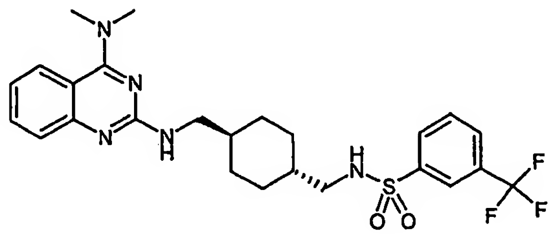
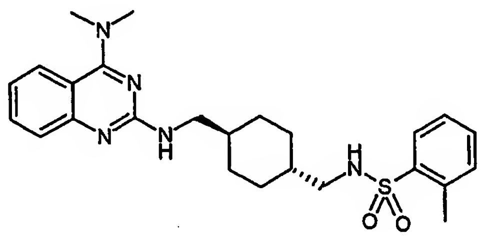
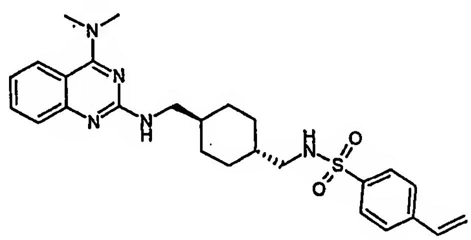
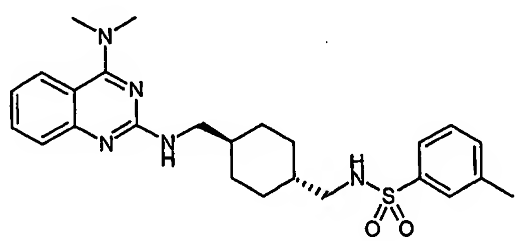
Example No.	Structure	APCI-MS
142		601 (M + H)
143		522 (M + H)
144		528 (M + H)
145		514 (M + H)
146		482 (M + H)

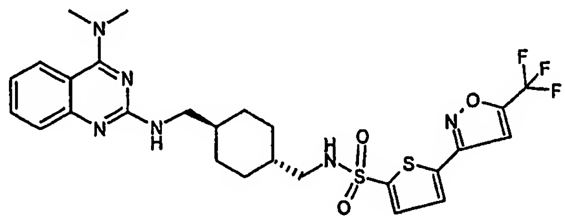
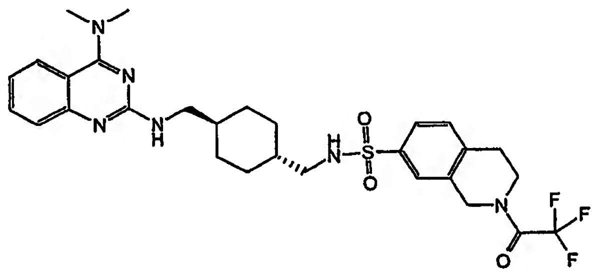
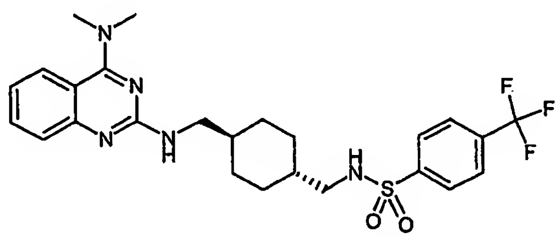
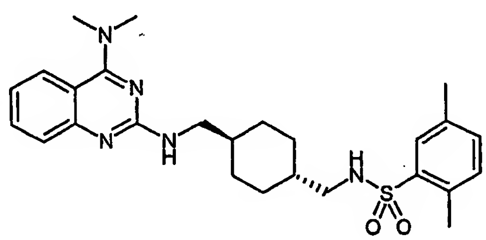
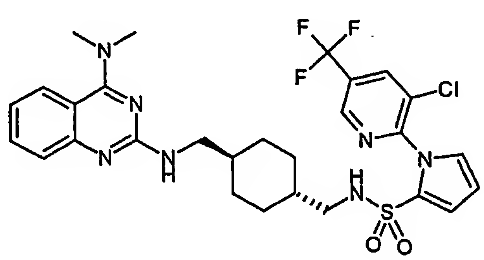
Example No.	Structure	APCI-MS
147		527 (M + H)
148		496 (M + H)
149		484 (M + H)
150		513 (M + H)
151		529 (M + H)

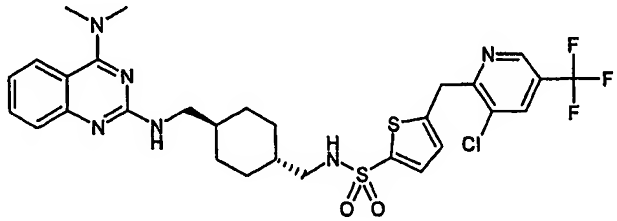
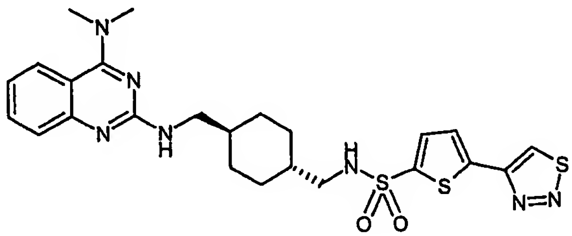
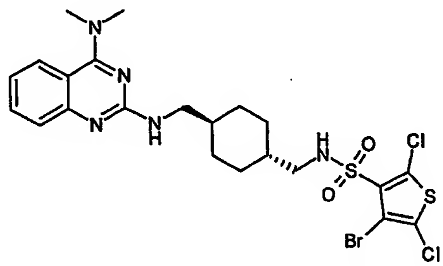
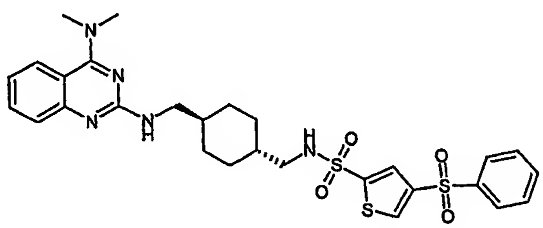
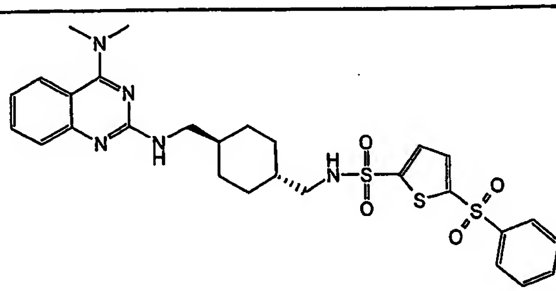
Example No.	Structure	APCI-MS
152		532 (M + H)
153		557 (M + H)
154		532 (M + H)
155		458 (M + H)
156		499 (M + H)

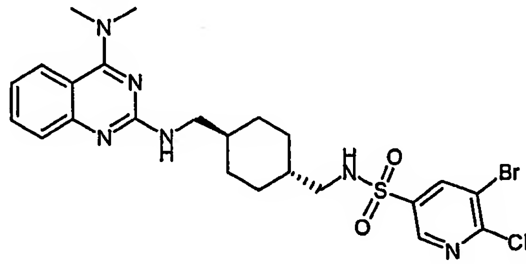
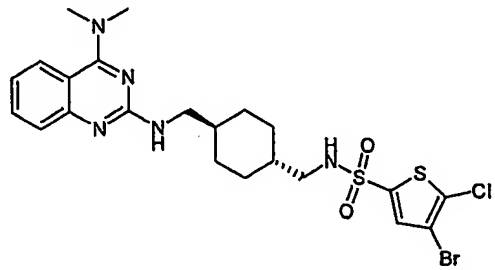
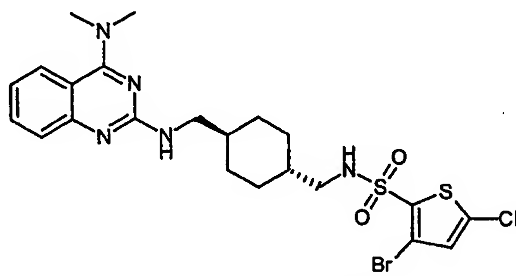
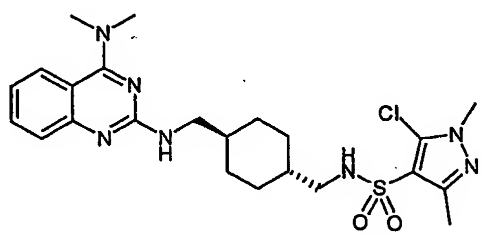
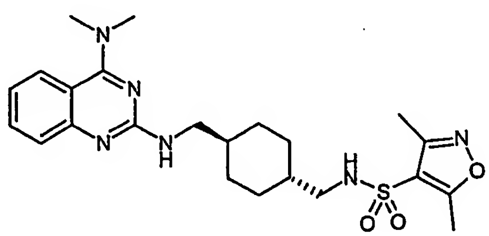
Example No.	Structure	APCI-MS
157		499 (M + H)
158		499 (M + H)
159		567 (M + H)
160		490 (M + H)
161		544 (M + H)

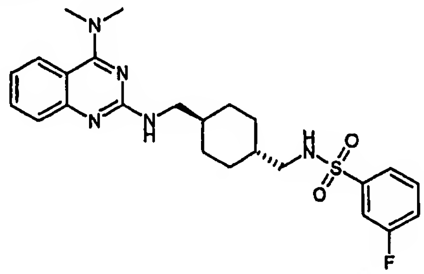
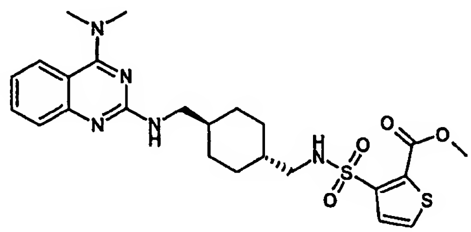
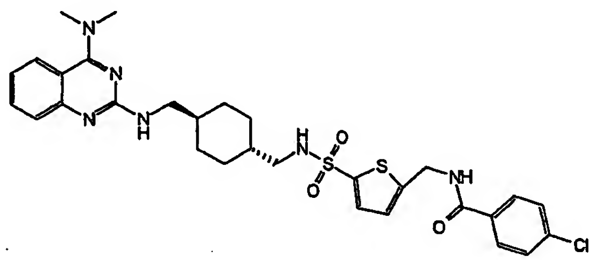
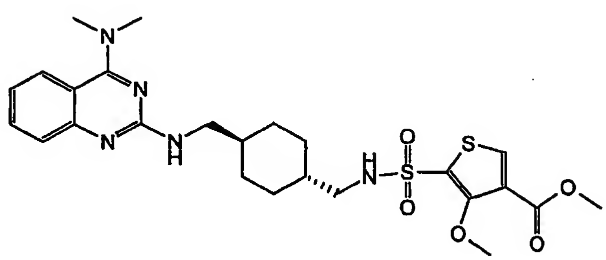
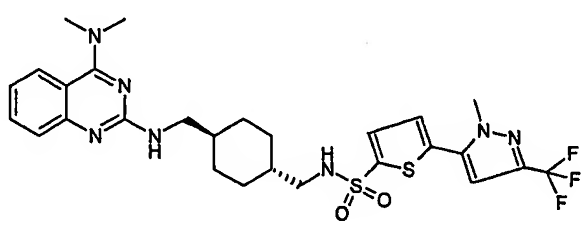
Example No.	Structure	APCI-MS
162		580 (M + H)
163		558 (M + H)
164		505 (M + H)
165		460 (M + H)
166		556 (M + H)

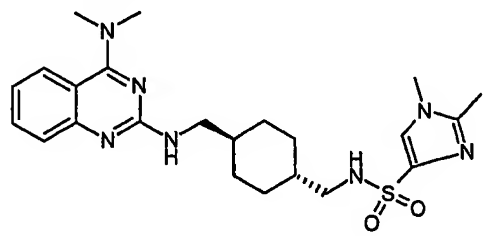
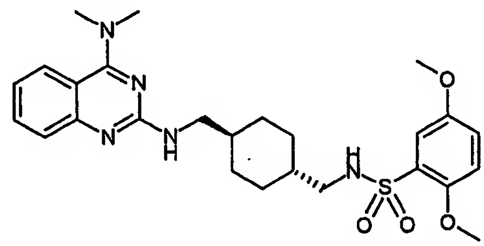
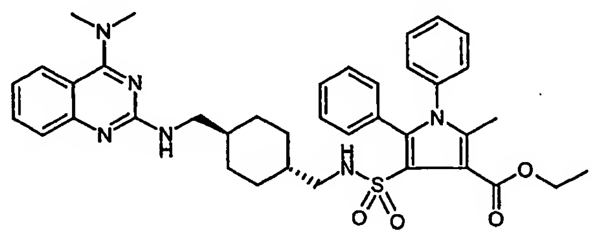
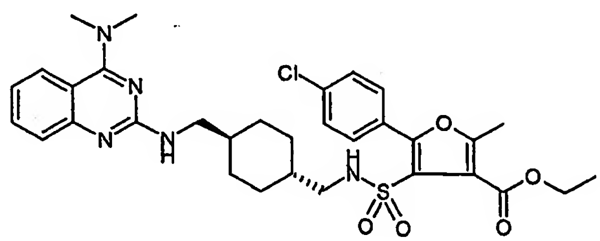
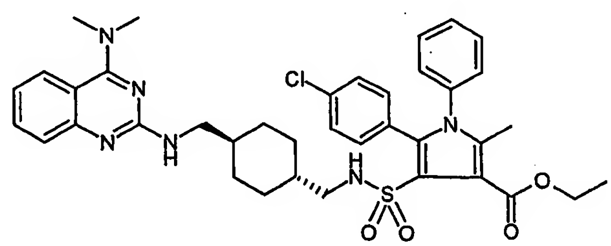
Example No.	Structure	APCI-MS
167		580 (M + H)
168		522 (M + H)
169		468 (M + H)
170		480 (M + H)
171		468 (M + H)

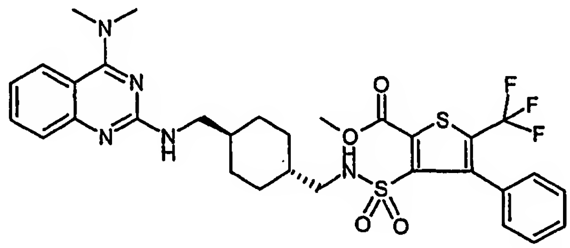
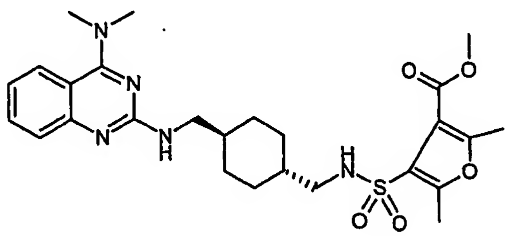
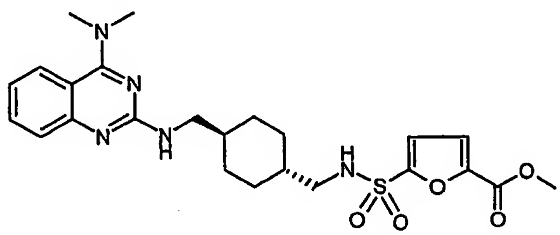
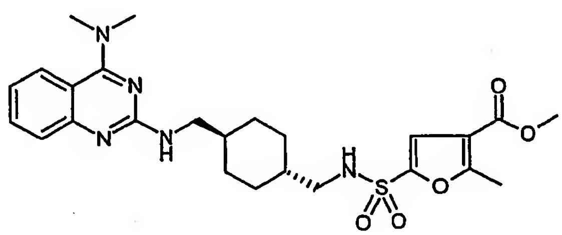
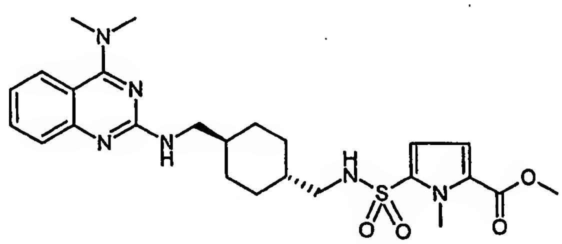
Example No.	Structure	APCI-MS
172		595 (M + H)
173		605 (M + H)
174		522 (M + H)
175		482 (M + H)
176		622 (M + H)

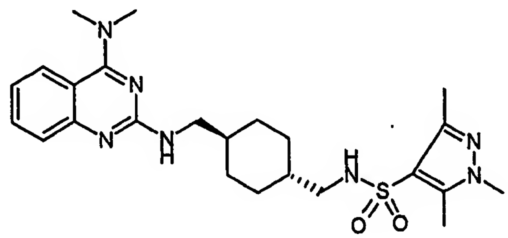
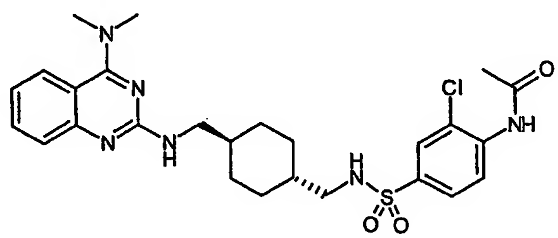
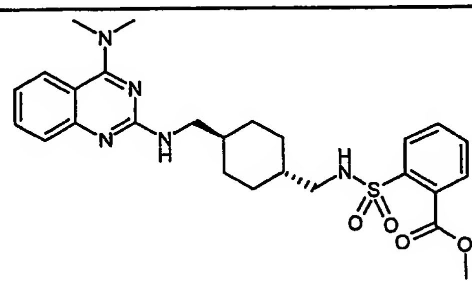
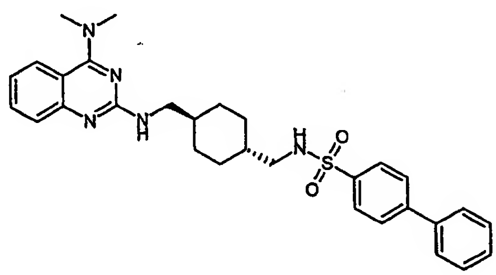
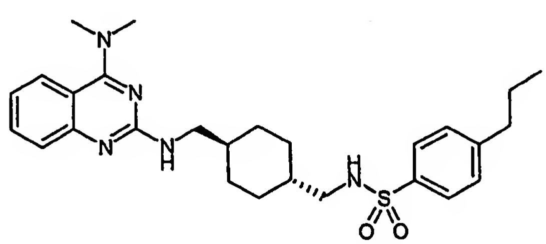
Example No.	Structure	APCI-MS
177		653 (M + H)
178		544 (M + H)
179		606 (M + H)
180		600 (M + H)
181		600 (M + H)

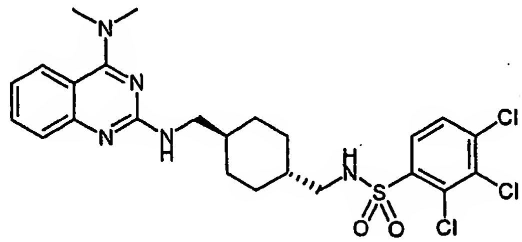
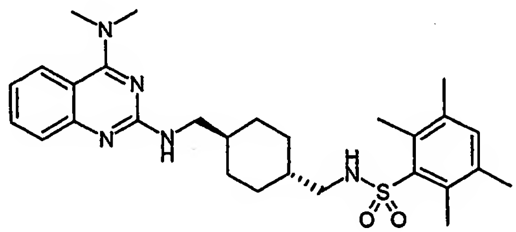
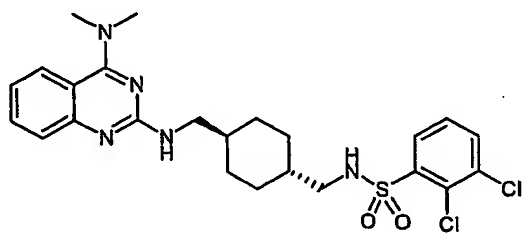
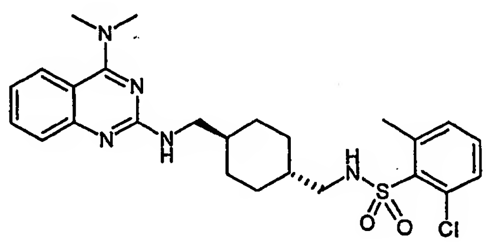
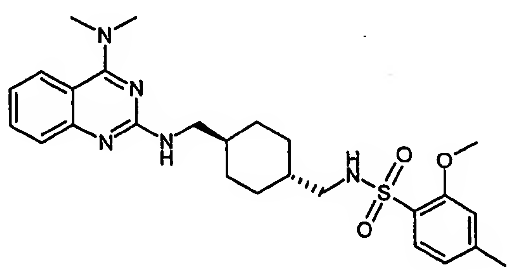
Example No.	Structure	APCI-MS
182		567 (M + H)
183		572 (M + H)
184		572 (M + H)
185		506 (M + H)
186		473 (M + H)

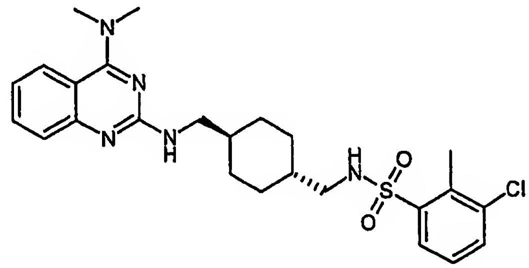
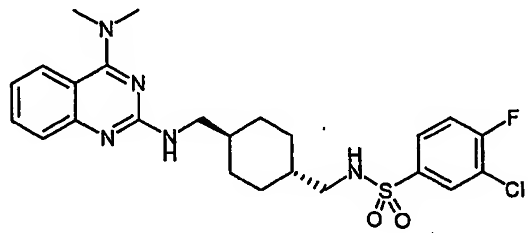
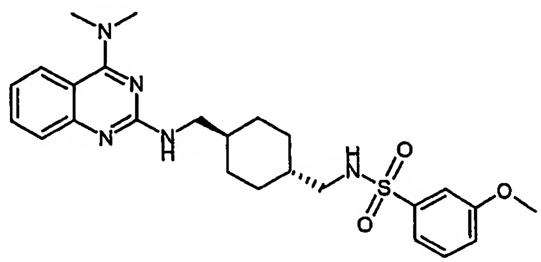
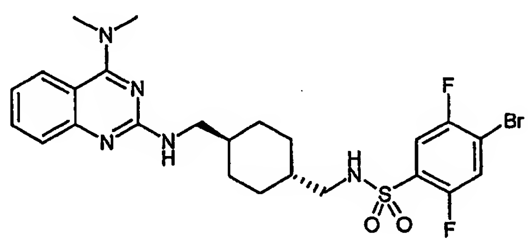
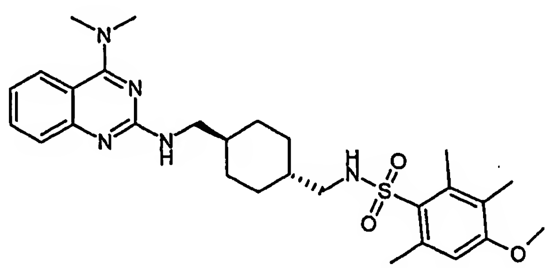
Example No.	Structure	APCI-MS
187		472 (M + H)
188		518 (M + H)
189		627 (M + H)
190		548 (M + H)
191		608 (M + H)

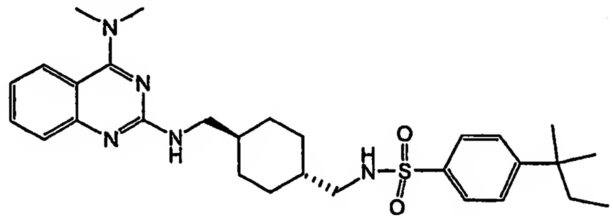
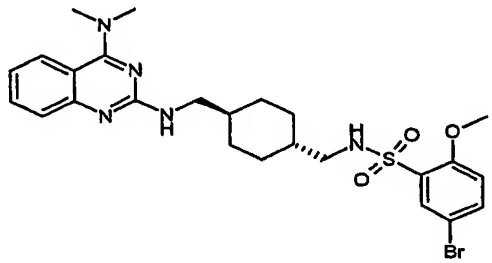
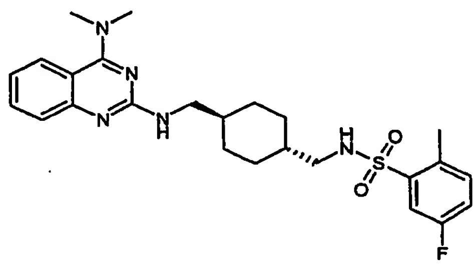
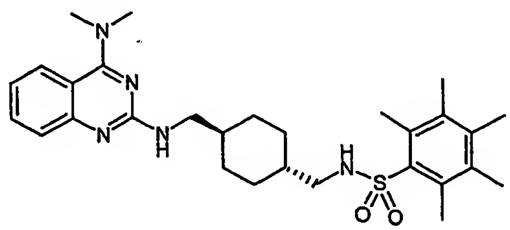
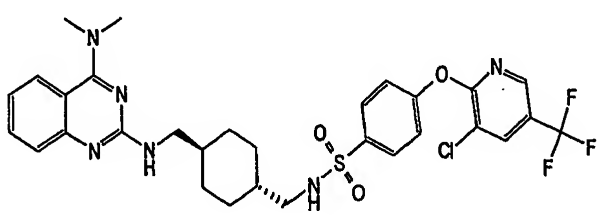
Example No.	Structure	APCI-MS
192		472 (M + H)
193		514 (M + H)
194		681 (M + H)
195		640 (M + H)
196		715 (M + H)

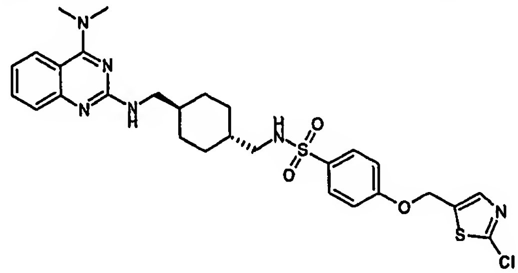
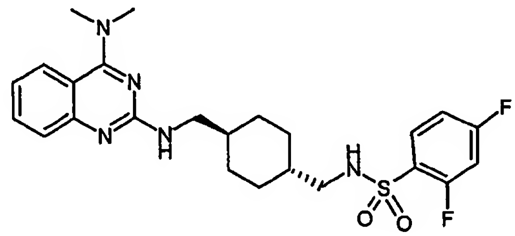
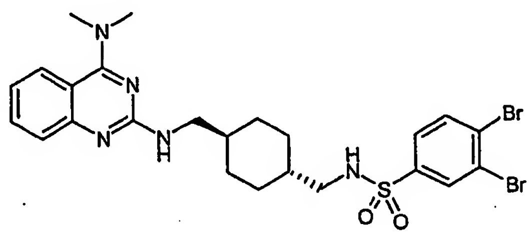
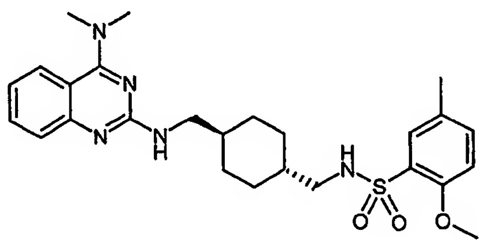
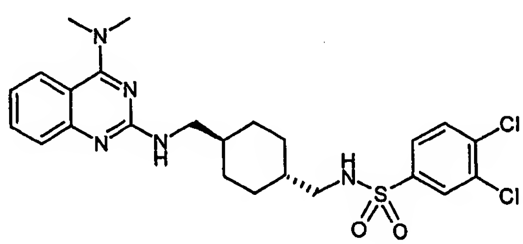
Example No.	Structure	APCI-MS
197		662 (M + H)
198		530 (M + H)
199		502 (M + H)
200		516 (M + H)
201		515 (M + H)

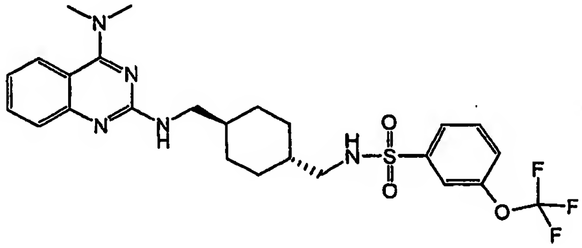
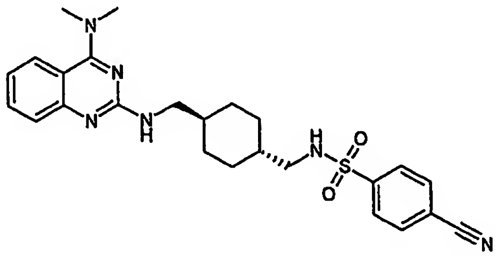
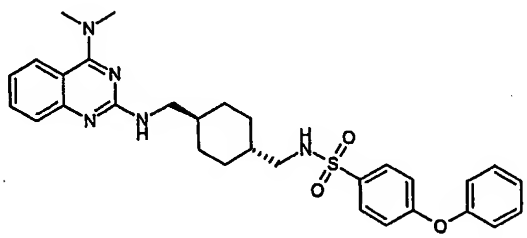
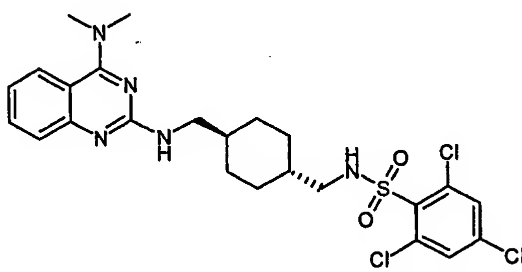
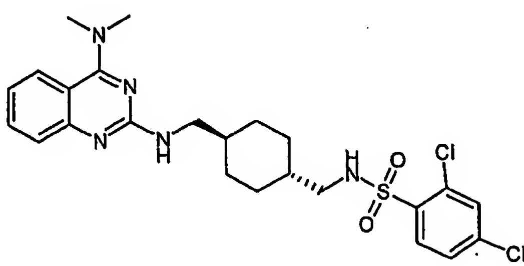
Example No.	Structure	APCI-MS
202		486 (M + H)
203		545 (M + H)
204		512 (M + H)
205		530 (M + H)
206		496 (M + H)

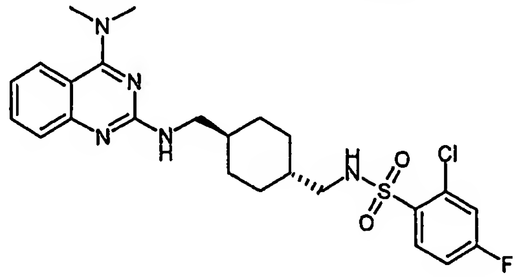
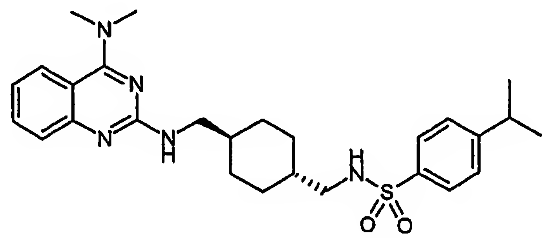
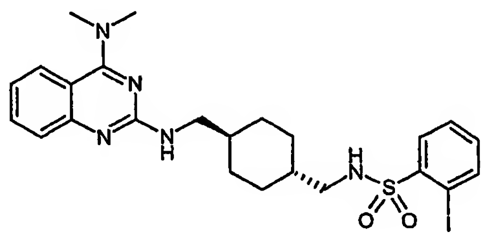
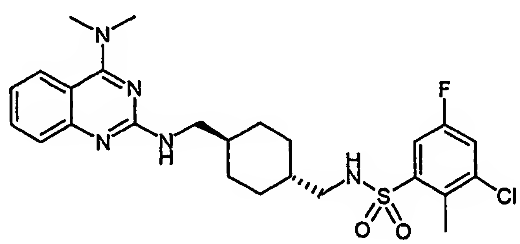
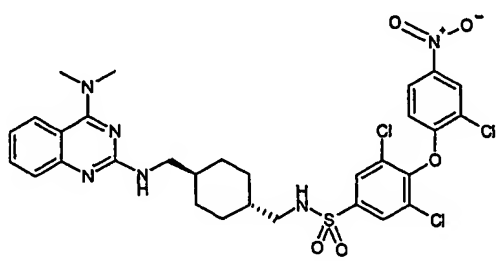
Example No.	Structure	APCI-MS
207		556 (M + H)
208		510 (M + H)
209		522 (M + H)
210		502 (M + H)
211		498 (M + H)

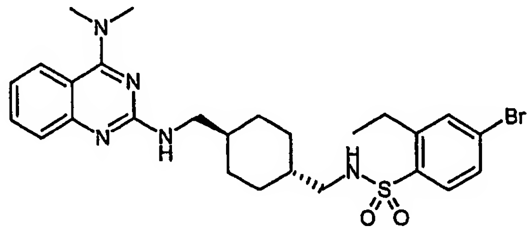
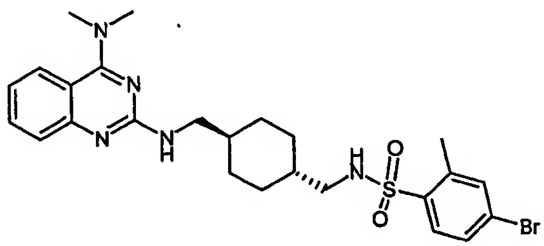
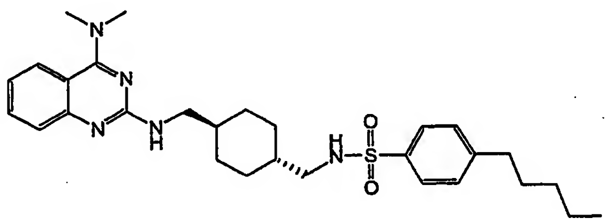
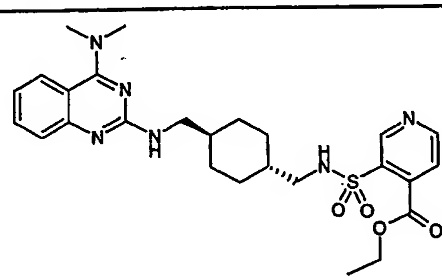
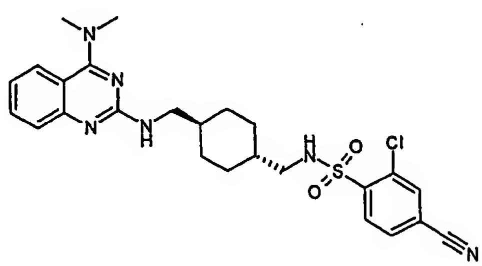
Example No.	Structure	APCI-MS
212		502 (M + H)
213		506 (M + H)
214		484 (M + H)
215		568 (M + H)
216		526 (M + H)

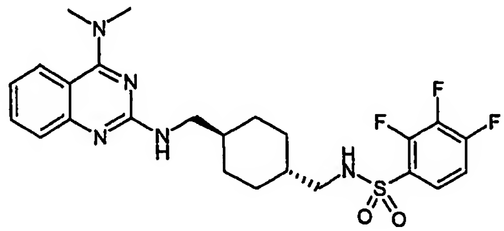
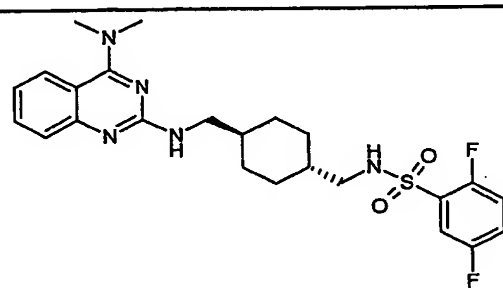
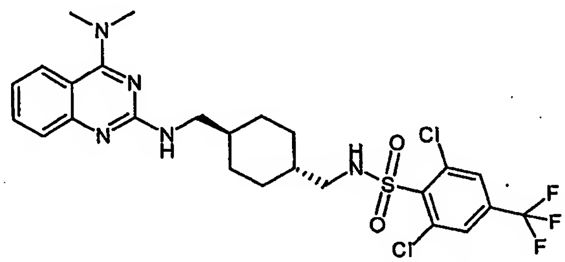
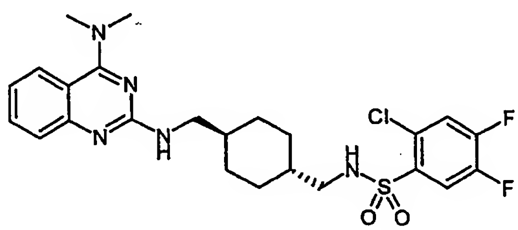
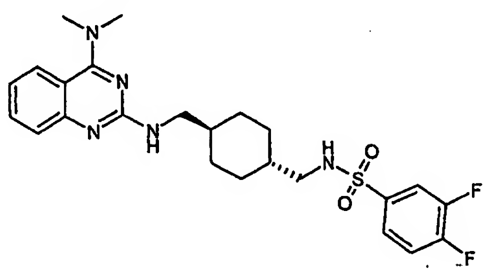
Example No.	Structure	APCI-MS
217		524 (M + H)
218		562 (M + H)
219		486 (M + H)
220		524 (M + H)
221		649 (M + H)

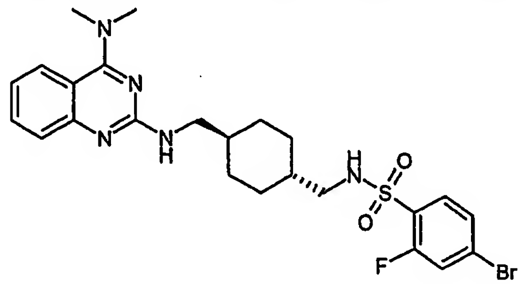
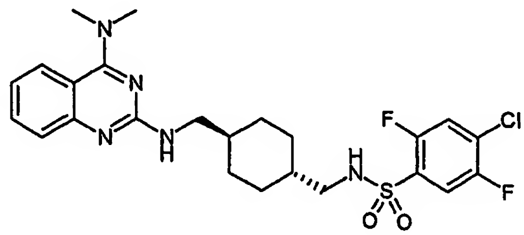
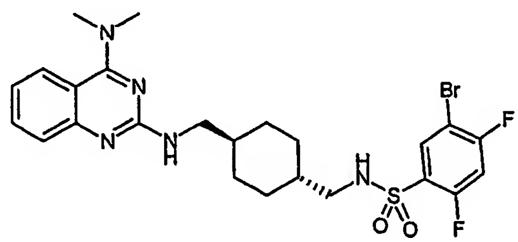
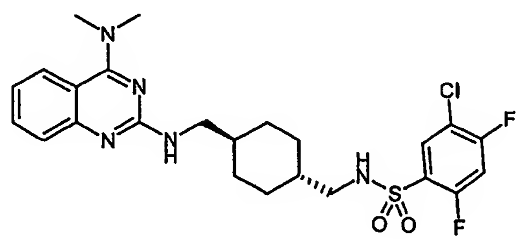
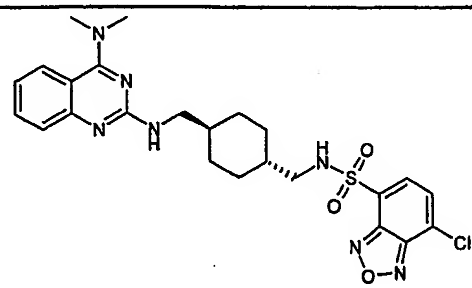
Example No.	Structure	APCI-MS
222		601 (M + H)
223		490 (M + H)
224		610 (M + H)
225		498 (M + H)
226		522 (M + H)

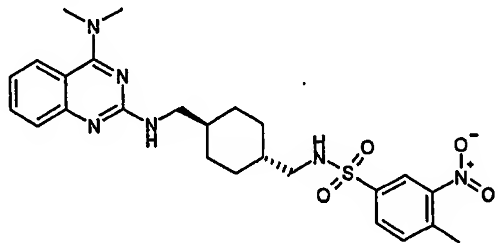
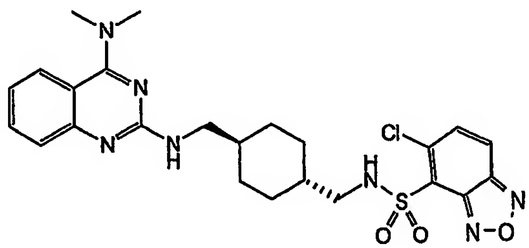
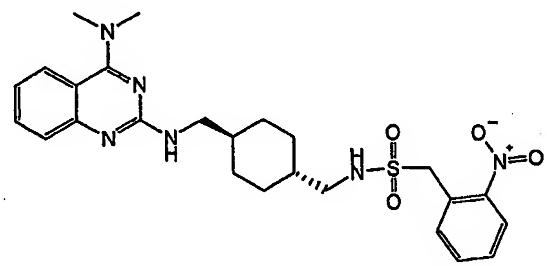
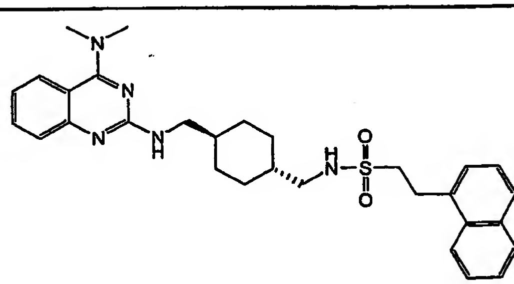
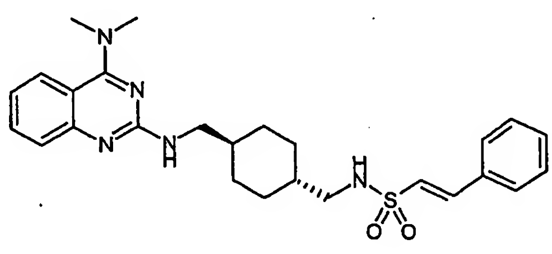
Example No.	Structure	APCI-MS
227		538 (M + H)
228		479 (M + H)
229		546 (M + H)
230		556 (M + H)
231		522 (M + H)

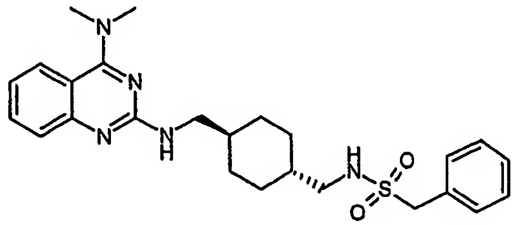
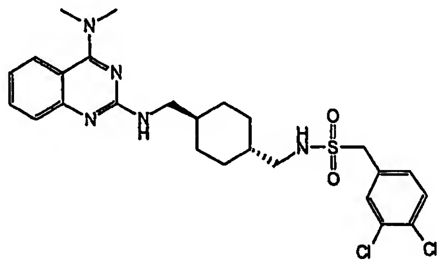
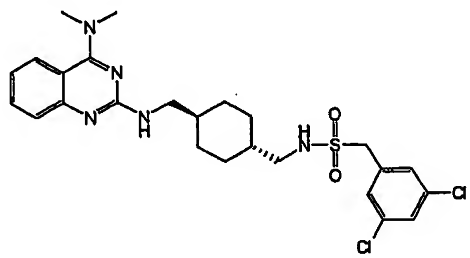
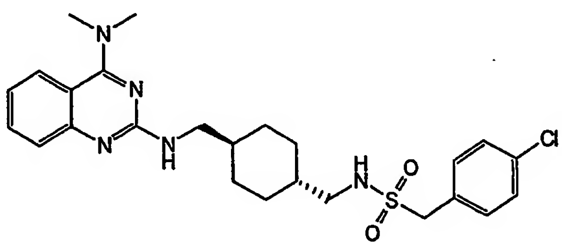
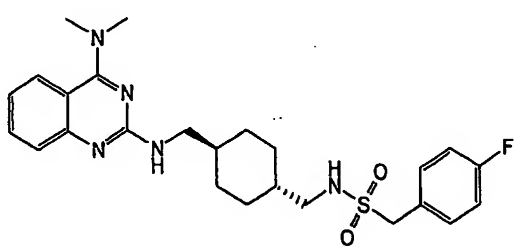
Example No.	Structure	APCI-MS
232		506 (M + H)
233		496 (M + H)
234		580 (M + H)
235		520 (M + H)
236		693 (M + H)

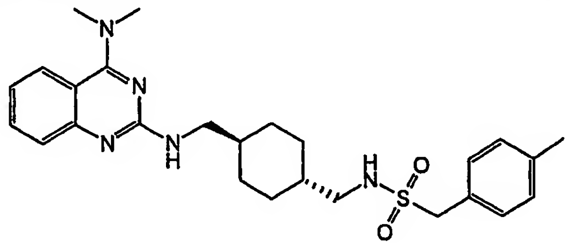
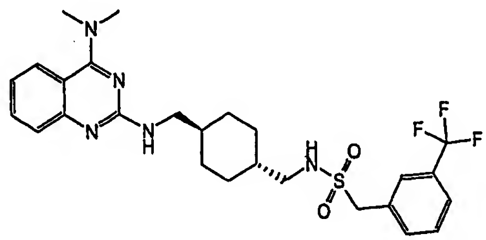
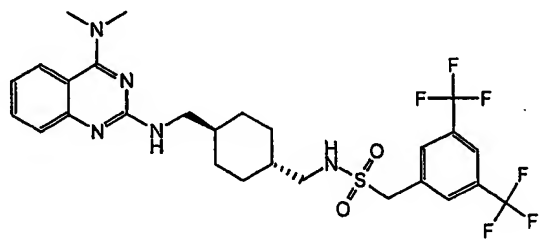
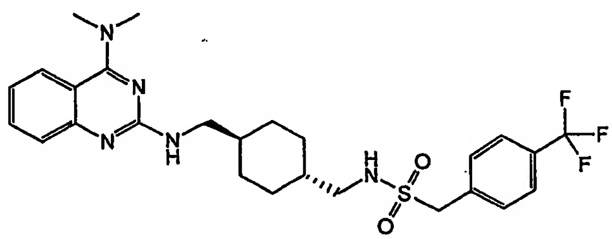
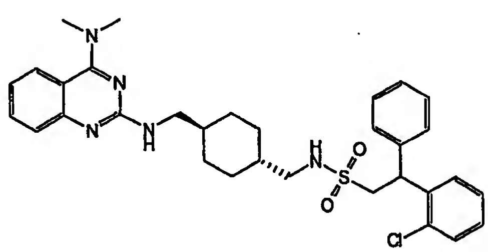
Example No.	Structure	APCI-MS
237		560 (M + H)
238		546 (M + H)
239		524 (M + H)
240		527 (M + H)
241		513 (M + H)

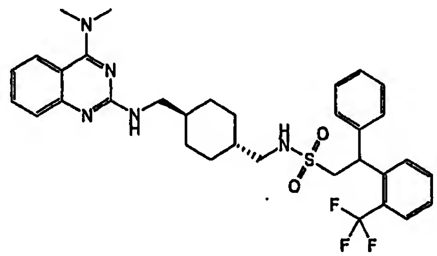
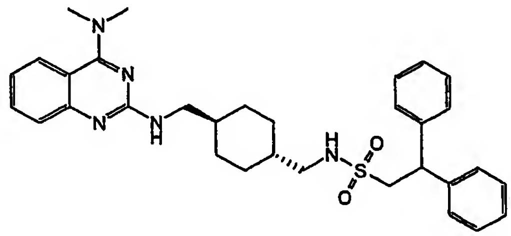
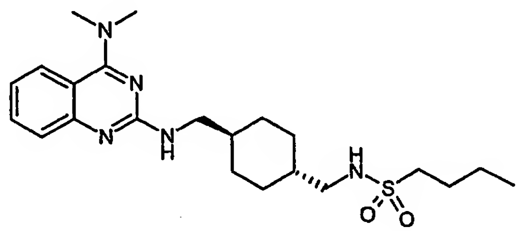
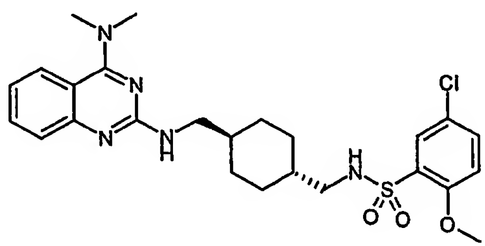
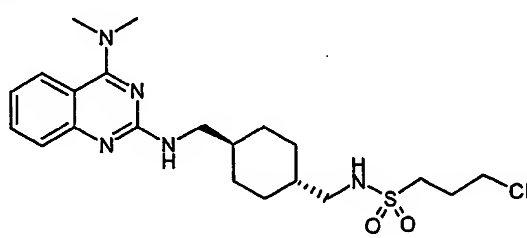
Example No.	Structure	APCI-MS
242		508 (M + H)
243		490 (M + H)
244		590 (M + H)
245		524 (M + H)
246		490 (M + H)

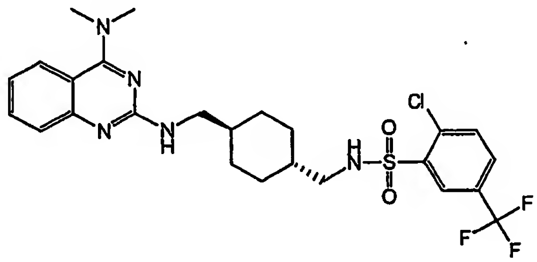
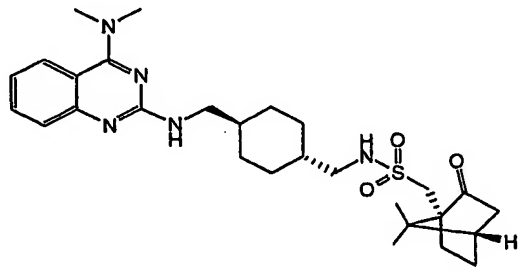
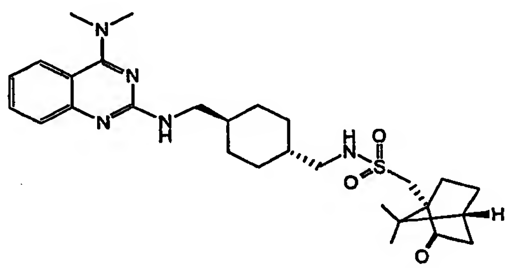
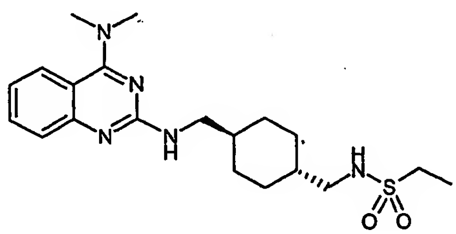
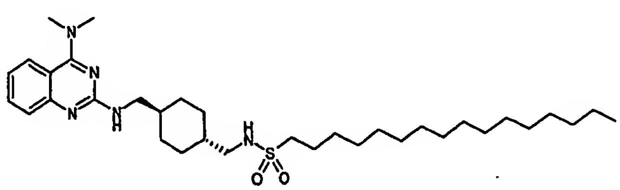
Example No.	Structure	APCI-MS
247		550 (M + H)
248		524 (M + H)
249		568 (M + H)
250		524 (M + H)
251		530 (M + H)

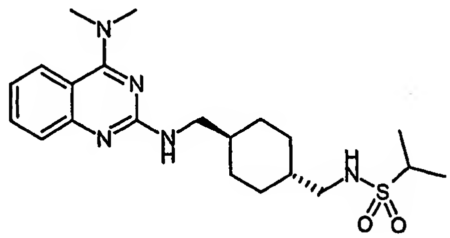
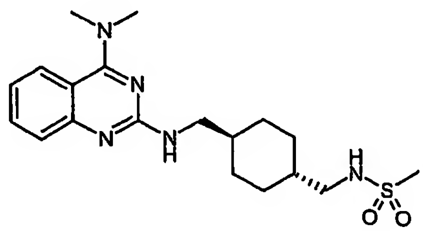
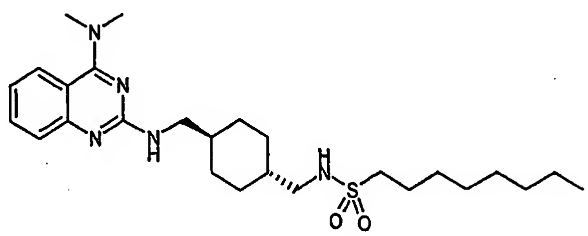
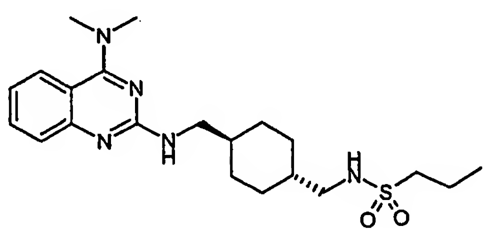
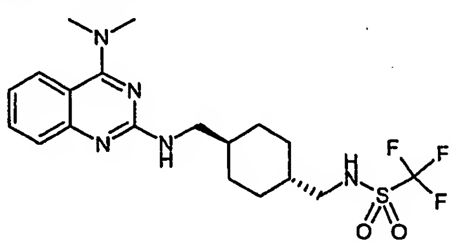
Example No.	Structure	APCI-MS
252		513 (M + H)
253		530 (M + H)
254		513 (M + H)
255		532 (M + H)
256		480 (M + H)

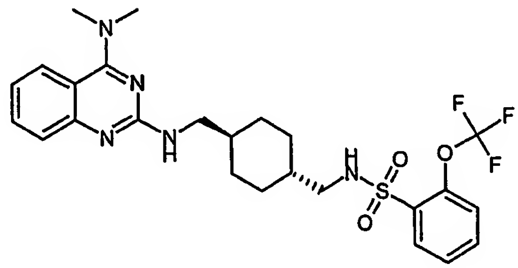
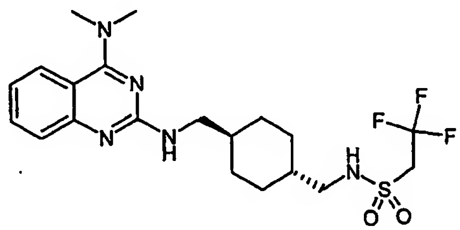
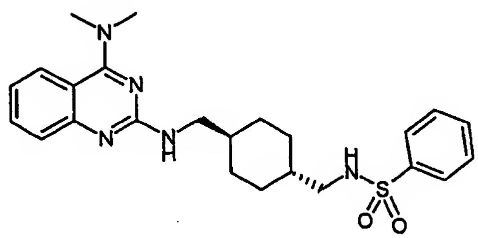
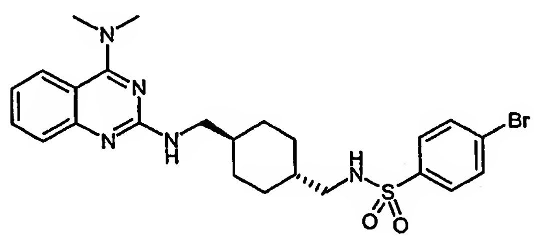
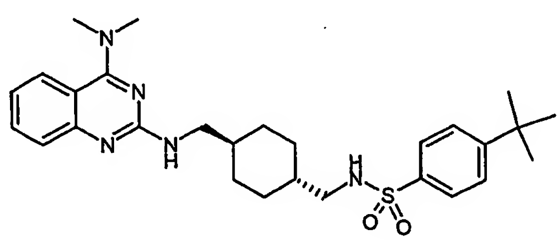
Example No.	Structure	APCI-MS
257		468 (M + H)
258		536 (M + H)
259		536 (M + H)
260		502 (M + H)
261		486 (M + H)

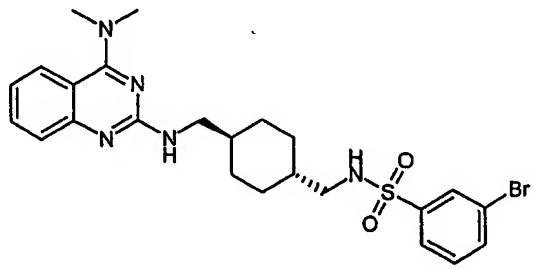
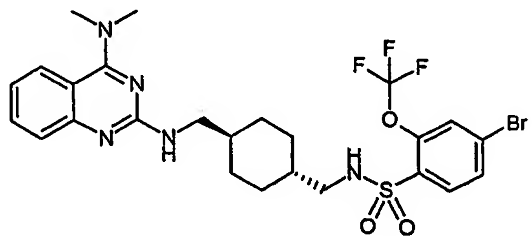
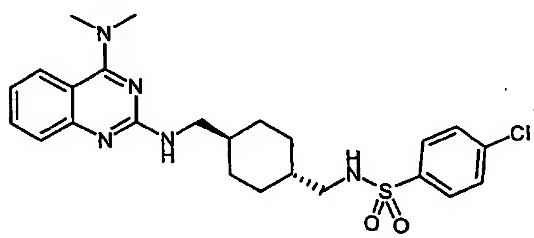
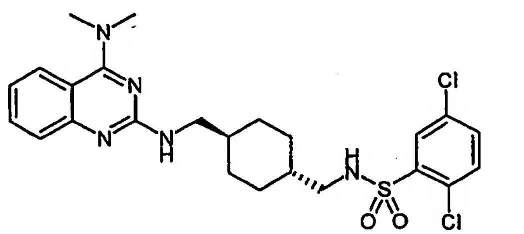
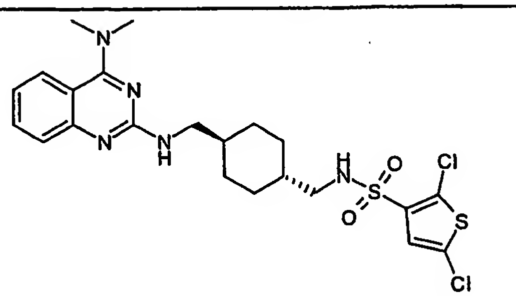
Example No.	Structure	APCI-MS
262		482 (M + H)
263		536 (M + H)
264		604 (M + H)
265		536 (M + H)
266		592 (M + H)

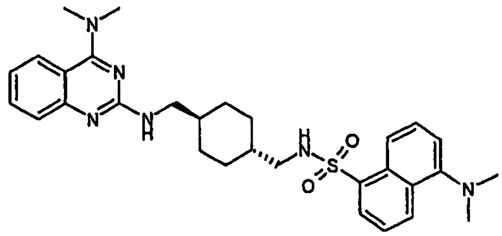
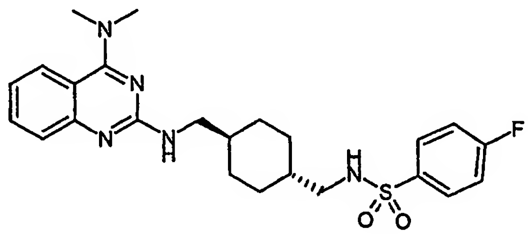
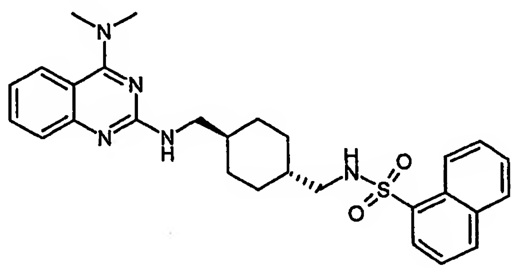
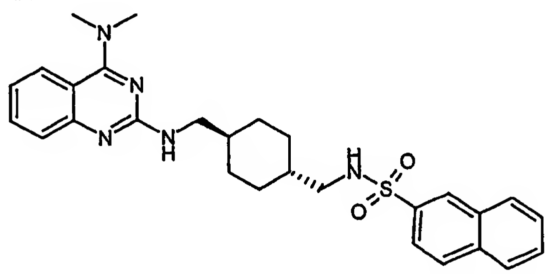
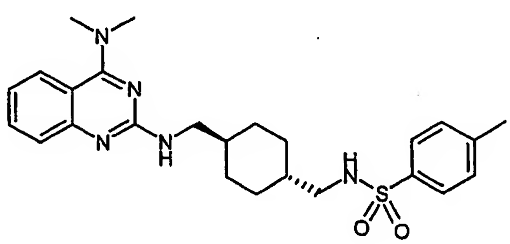
Example No.	Structure	APCI-MS
267		626 (M + H)
268		558 (M + H)
269		434 (M + H)
270		518 (M + H)
271		454 (M + H)

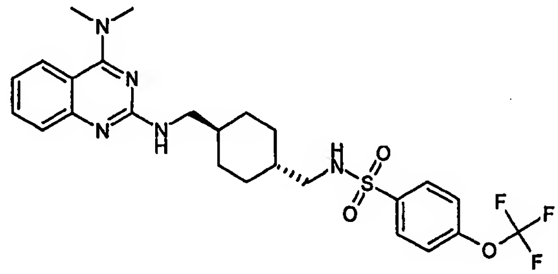
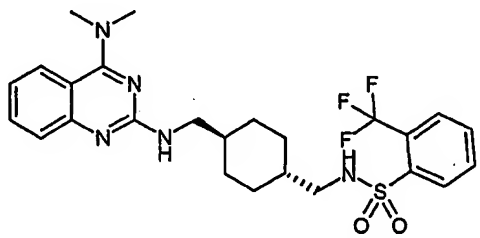
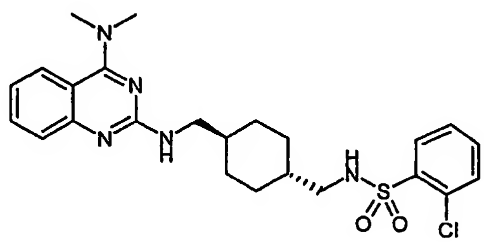
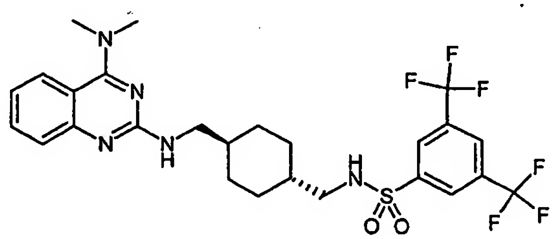
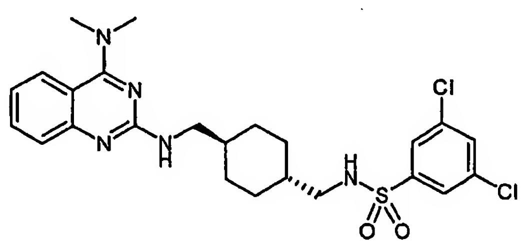
Example No.	Structure	APCI-MS
272		556 (M + H)
273		528 (M + H)
274		528 (M + H)
275		406 (M + H)
276		602 (M + H)

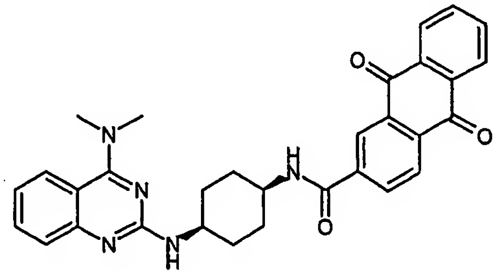
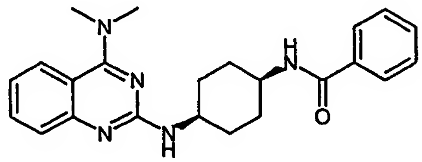
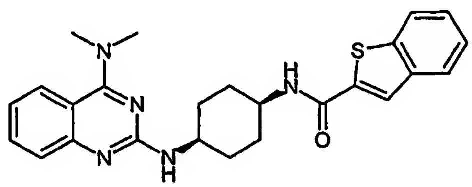
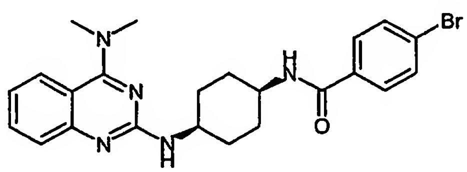
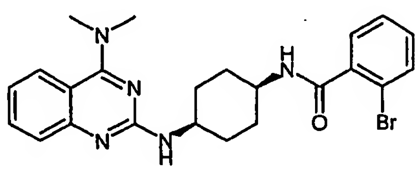
Example No.	Structure	APCI-MS
277		420 (M + H)
278		392 (M + H)
279		490 (M + H)
280		420 (M + H)
281		446 (M + H)

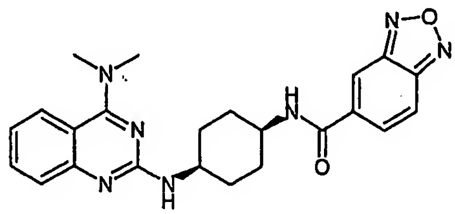
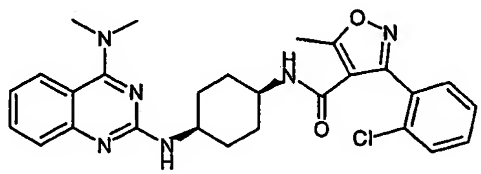
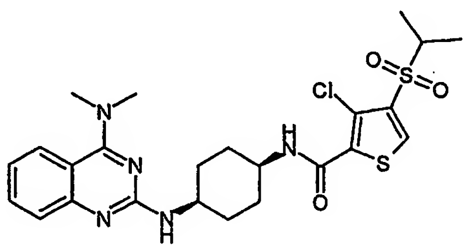
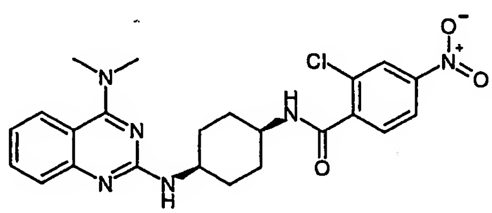
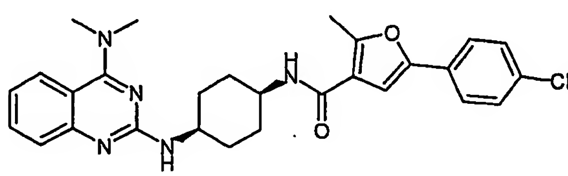
Example No.	Structure	APCI-MS
282		538 (M + H)
283		460 (M + H)
284		454 (M + H)
285		532 (M + H)
286		510 (M + H)

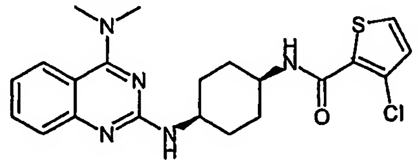
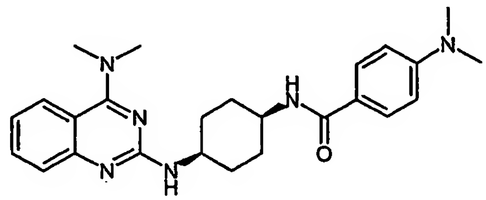
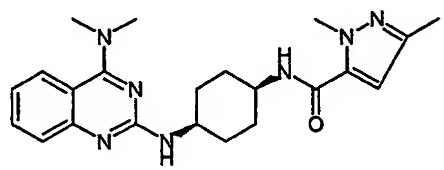
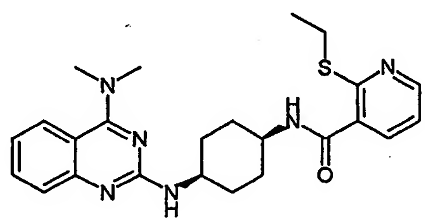
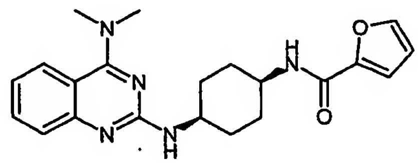
Example No.	Structure	APCI-MS
287		532 (M + H)
288		616 (M + H)
289		488 (M + H)
290		522 (M + H)
291		528 (M + H)

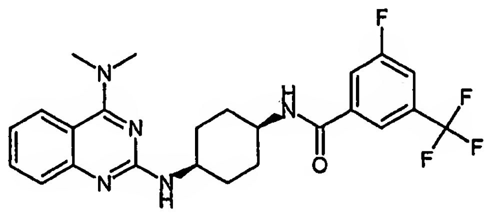
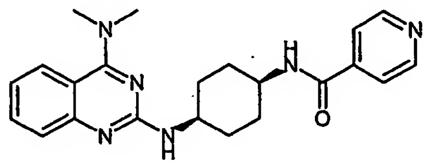
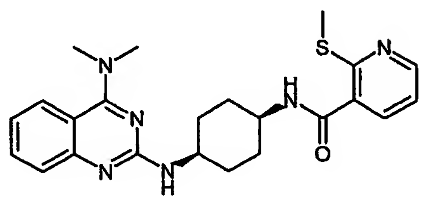
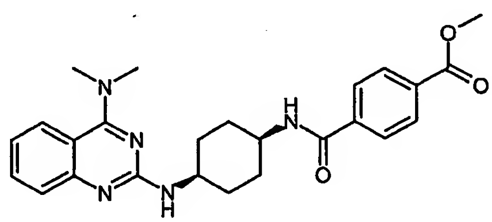
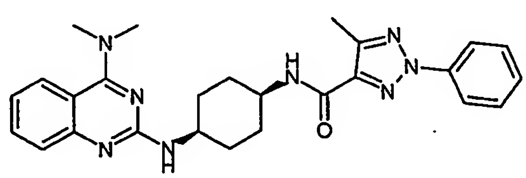
Example No.	Structure	APCI-MS
292		547 (M + H)
293		472 (M + H)
294		504 (M + H)
295		504 (M + H)
296		468 (M + H)

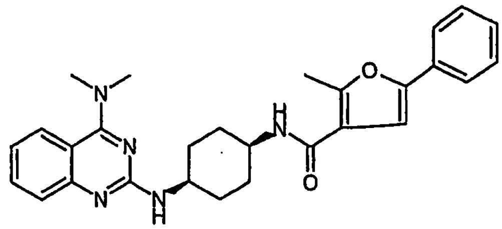
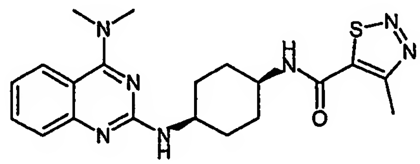
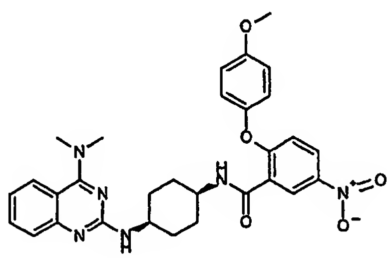
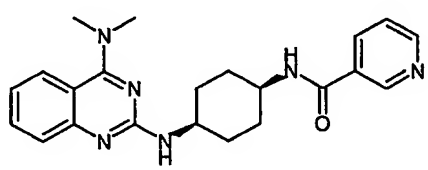
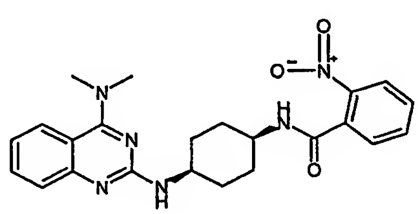
Example No.	Structure	APCI-MS
297		538 (M + H)
298		522 (M + H)
299		488 (M + H)
300		590 (M + H)
301		522 (M + H)

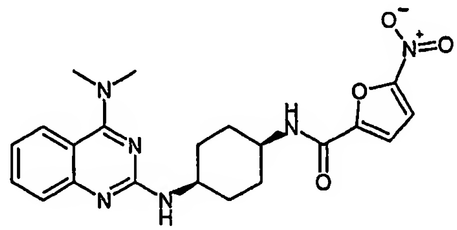
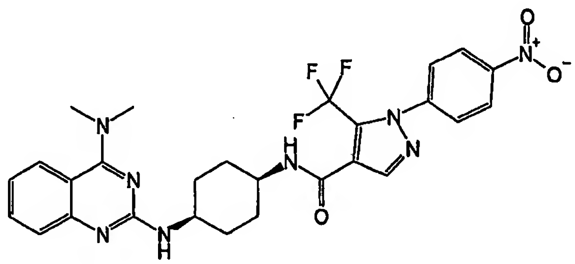
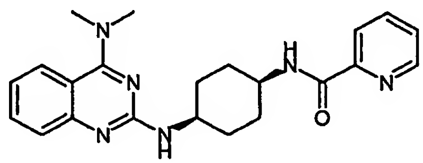
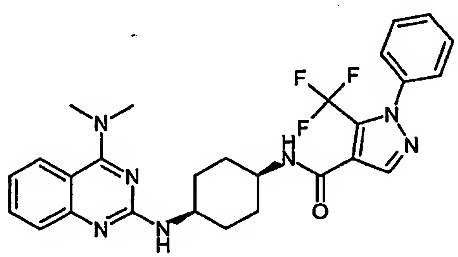
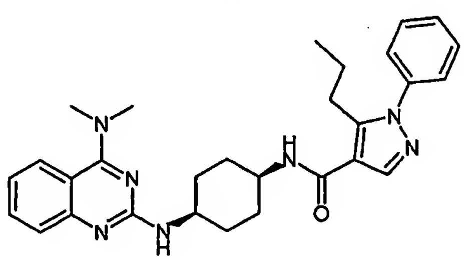
Example No.	Structure	APCI-MS
302		520 (M + H)
303		390 (M + H)
304		446 (M + H)
305		468 (M + H)
306		468 (M + H)

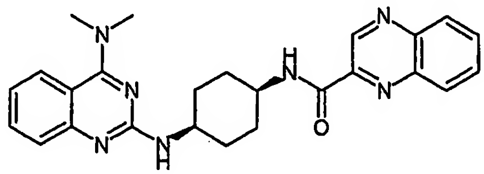
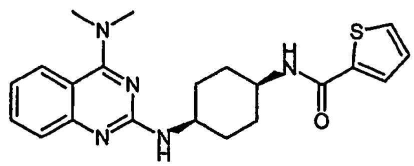
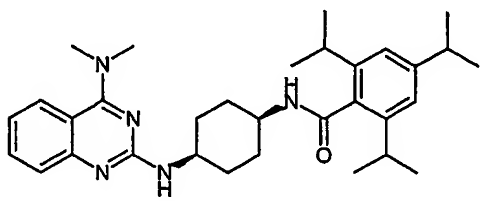
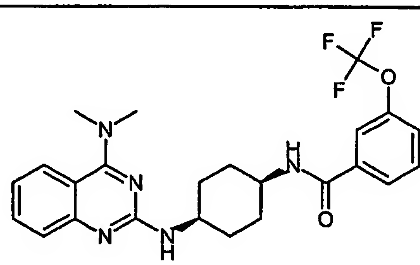
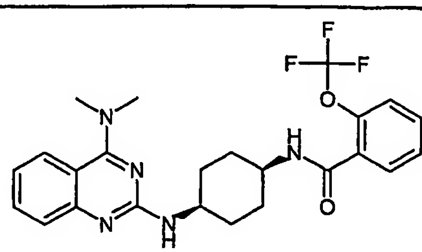
Example No.	Structure	APCI-MS
307		432 (M + H)
308		505 (M + H)
309		536 (M + H)
310		469 (M + H)
311		504 (M + H)

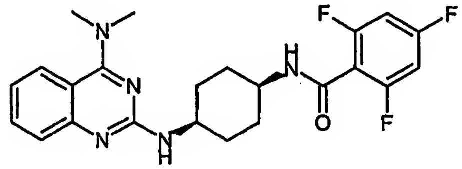
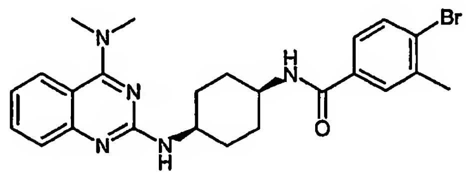
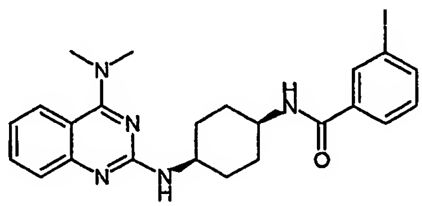
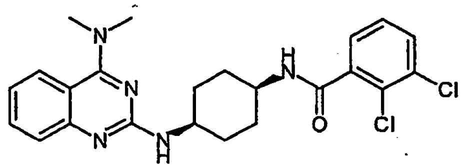
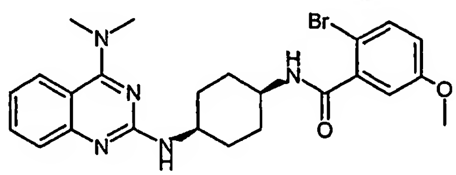
Example No.	Structure	APCI-MS
312		430 (M + H)
313		433 (M + H)
314		408 (M + H)
315		451 (M + H)
316		380 (M + H)

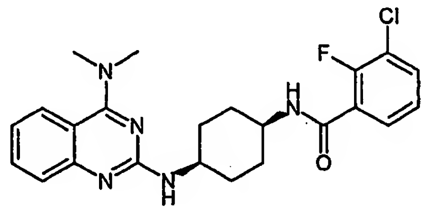
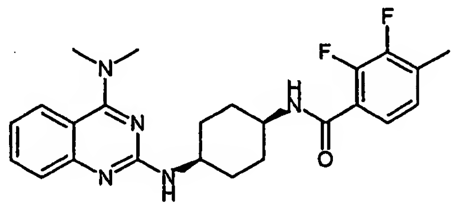
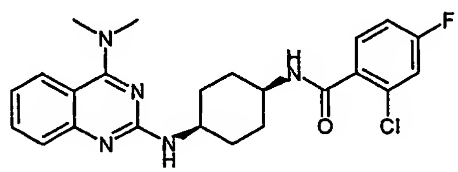
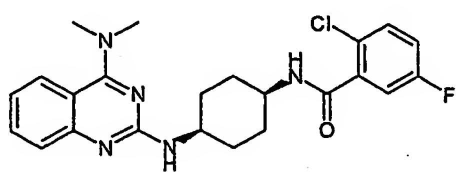
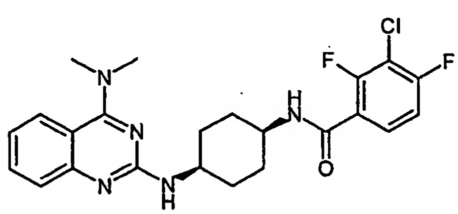
Example No.	Structure	APCI-MS
317		476 (M + H)
318		391 (M + H)
319		437 (M + H)
320		448 (M + H)
321		471 (M + H)

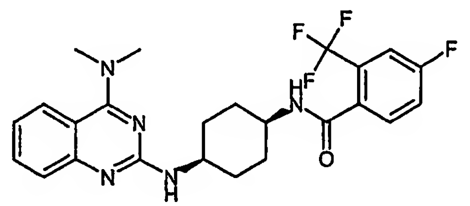
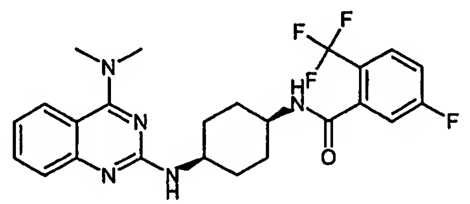
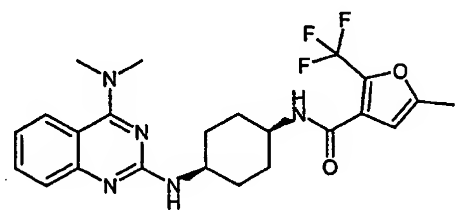
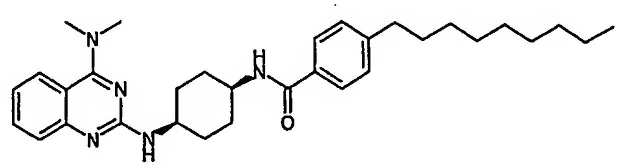
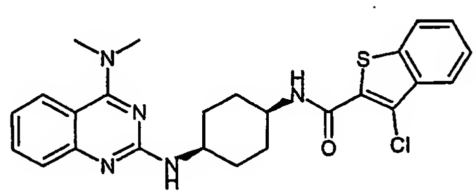
Example No.	Structure	APCI-MS
322		470 (M + H)
323		412 (M + H)
324		557 (M + H)
325		391 (M + H)
326		435 (M + H)

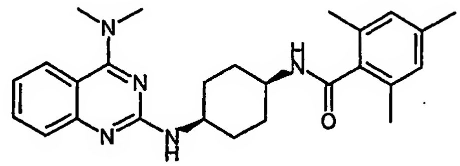
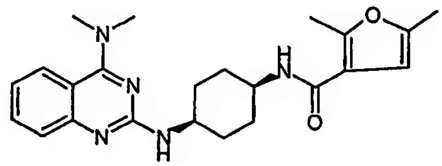
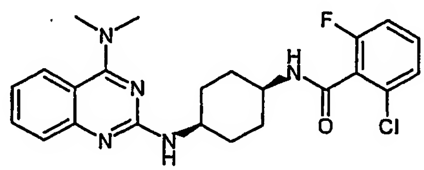
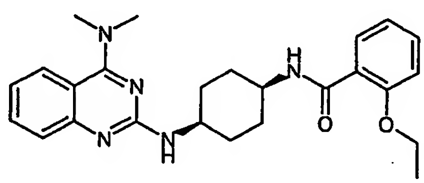
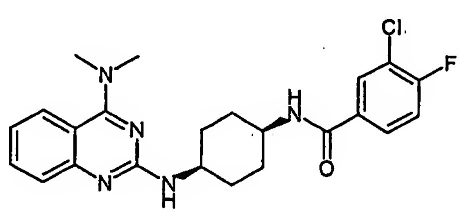
Example No.	Structure	APCI-MS
327		425 (M + H)
328		569 (M + H)
329		391 (M + H)
330		524 (M + H)
331		498 (M + H)

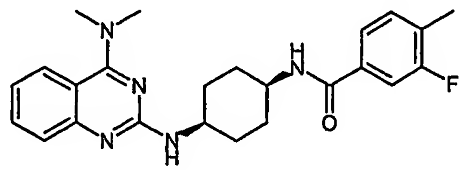
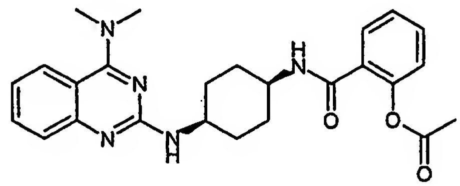
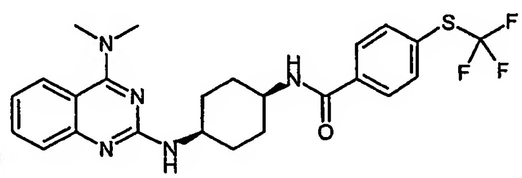
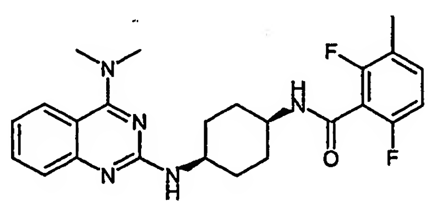
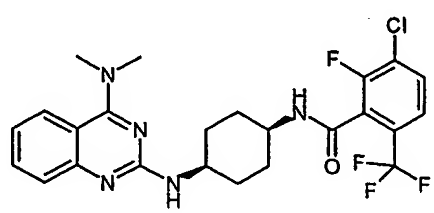
Example No.	Structure	APCI-MS
332		442 (M + H)
333		396 (M + H)
334		516 (M + H)
335		474 (M + H)
336		474 (M + H)

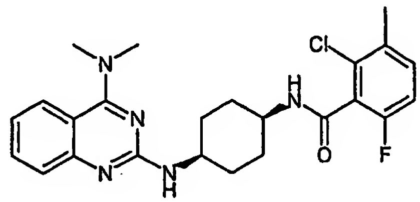
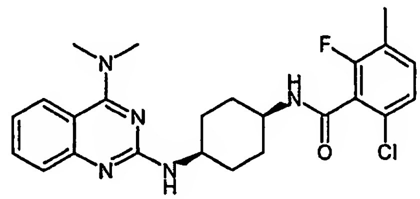
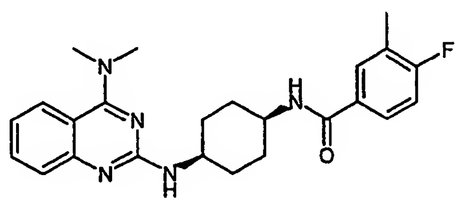
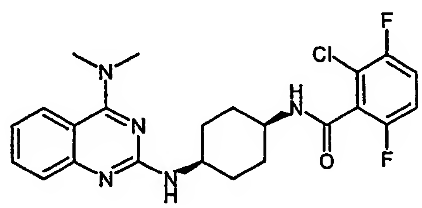
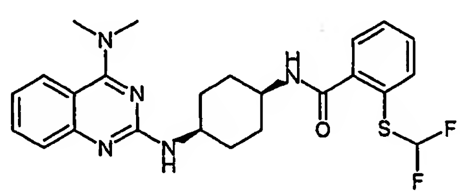
Example No.	Structure	APCI-MS
337		444 (M + H)
338		482 (M + H)
339		516 (M + H)
340		458 (M + H)
341		498 (M + H)

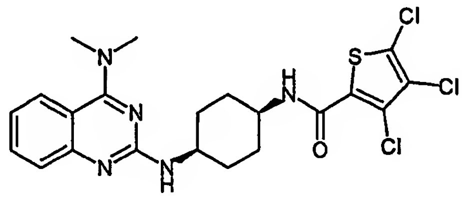
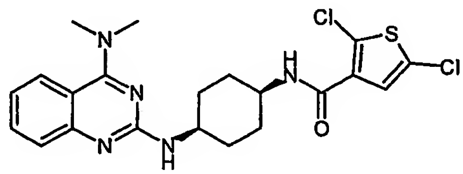
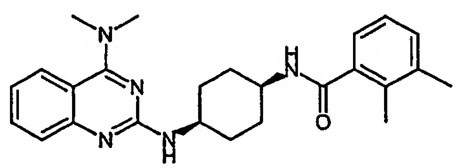
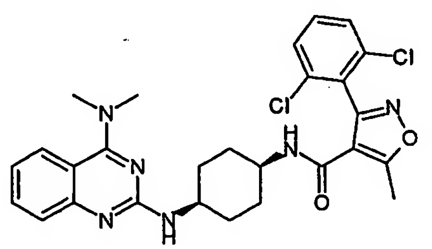
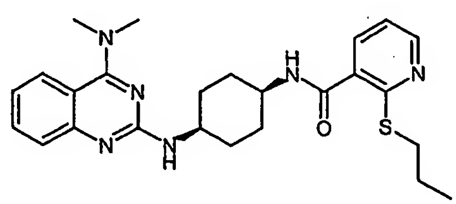
Example No.	Structure	APCI-MS
342		442 (M + H)
343		440 (M + H)
344		442 (M + H)
345		442 (M + H)
346		460 (M + H)

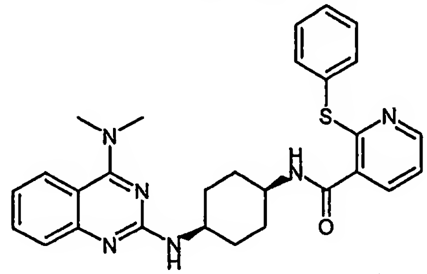
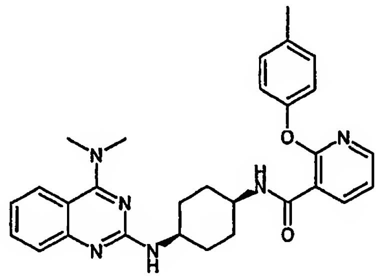
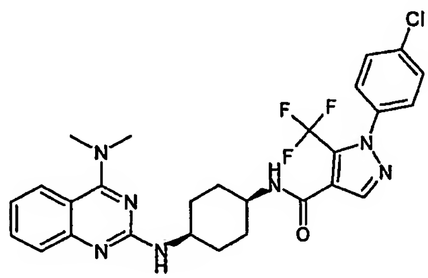
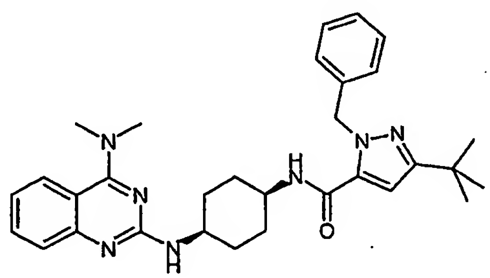
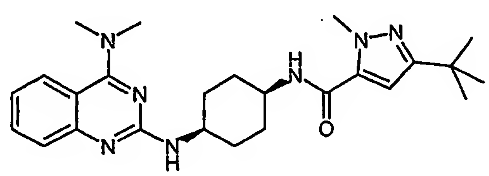
Example No.	Structure	APCI-MS
347		476 (M + H)
348		476 (M + H)
349		462 (M + H)
350		516 (M + H)
351		480 (M + H)

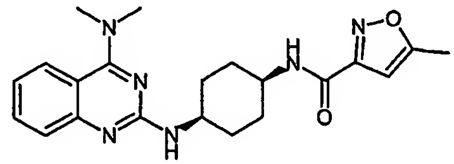
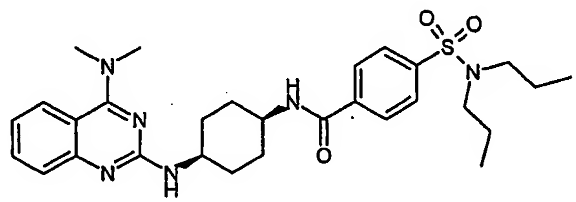
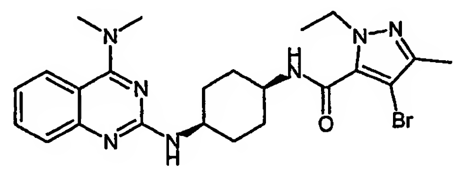
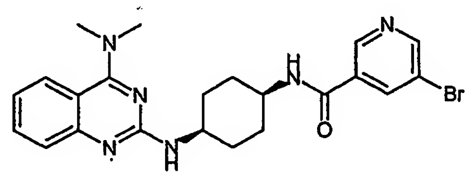
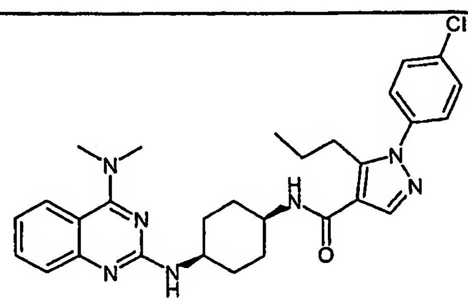
Example No.	Structure	APCI-MS
352		432 (M + H)
353		408 (M + H)
354		442 (M + H)
355		434 (M + H)
356		442 (M + H)

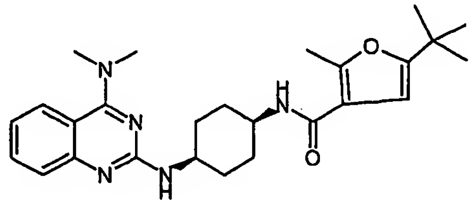
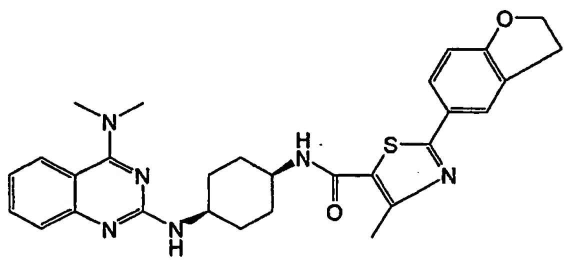
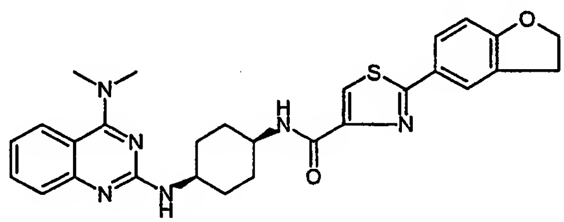
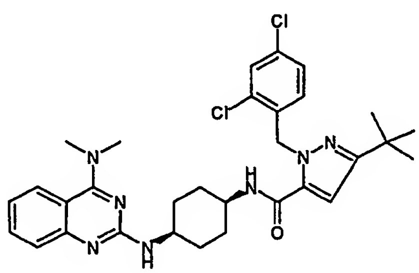
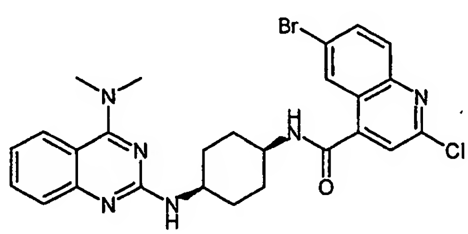
Example No.	Structure	APCI-MS
357		422 (M + H)
358		406 (M + H)
359		490 (M + H)
360		440 (M + H)
361		510 (M + H)

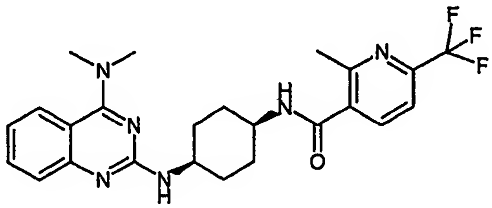
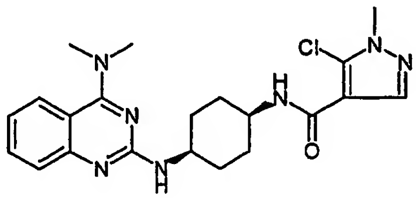
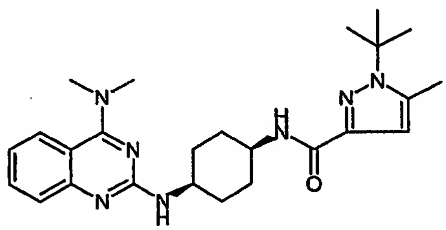
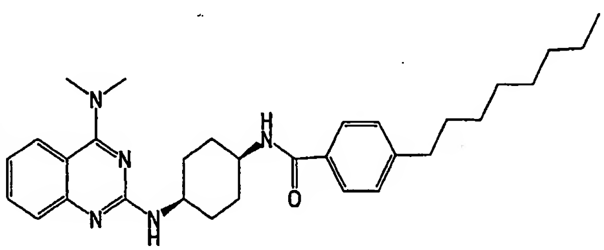
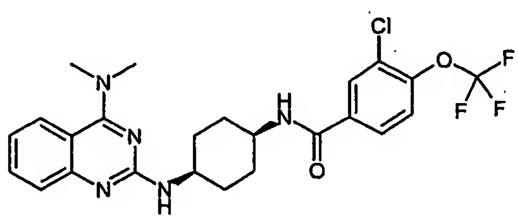
Example No.	Structure	APCI-MS
362		456 (M + H)
363		456 (M + H)
364		422 (M + H)
365		460 (M + H)
366		472 (M + H)

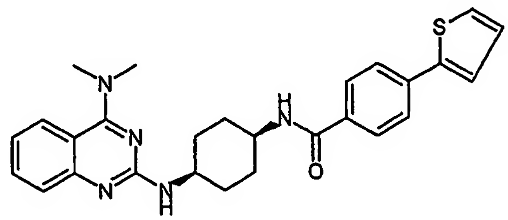
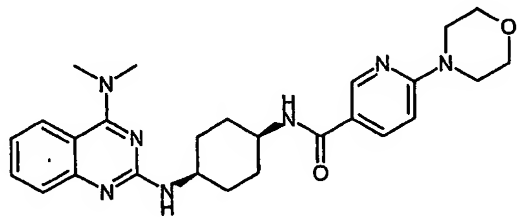
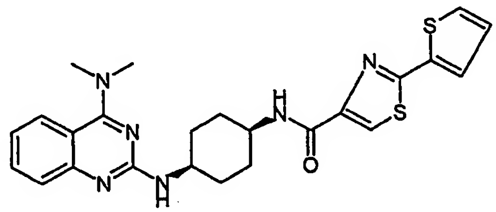
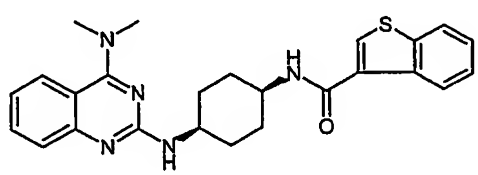
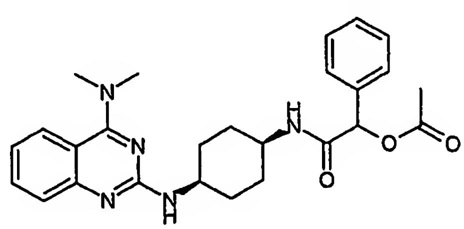
Example No.	Structure	APCI-MS
367		498 (M + H)
368		464 (M + H)
369		418 (M + H)
370		539 (M + H)
371		465 (M + H)

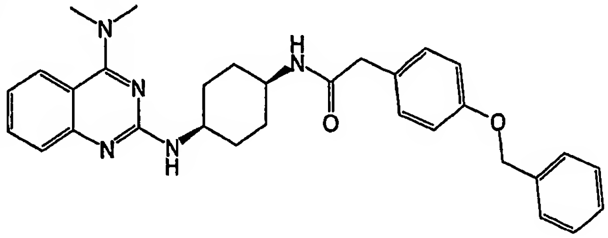
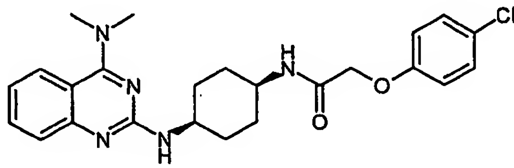
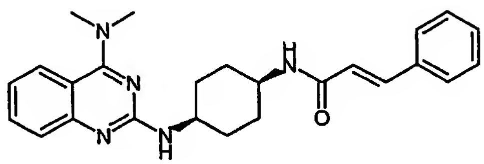
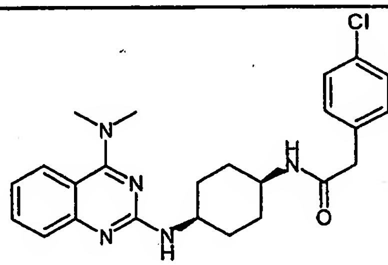
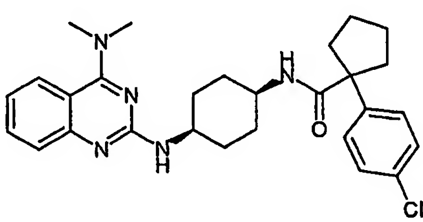
Example No.	Structure	APCI-MS
372		499 (M + H)
373		497 (M + H)
374		558 (M + H)
375		526 (M + H)
376		450 (M + H)

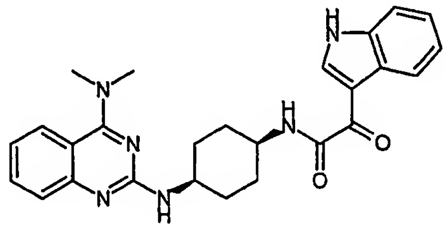
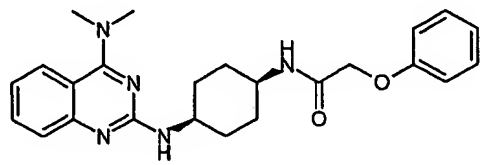
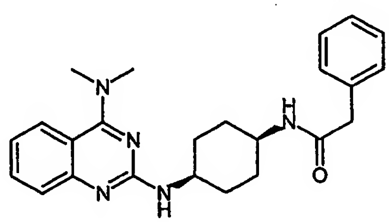
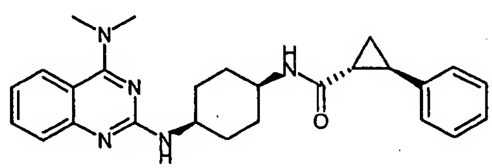
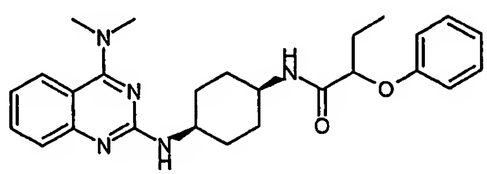
Example No.	Structure	APCI-MS
377		395 (M + H)
378		553 (M + H)
379		500 (M + H)
380		469 (M + H)
381		532 (M + H)

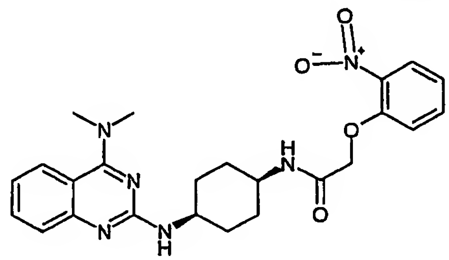
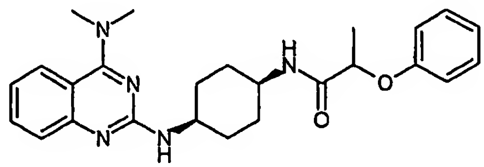
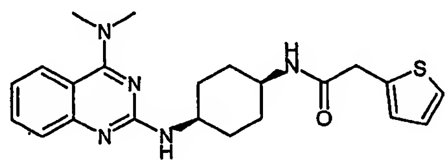
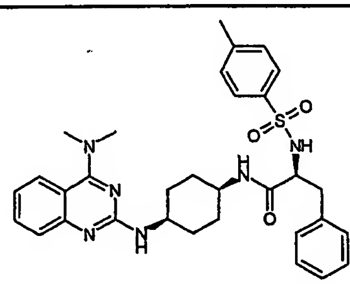
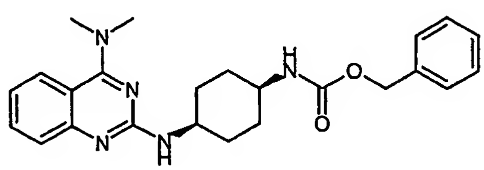
Example No.	Structure	APCI-MS
382		450 (M + H)
383		529 (M + H)
384		515 (M + H)
385		594 (M + H)
386		553 (M + H)

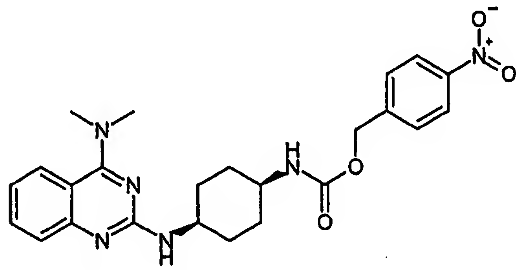
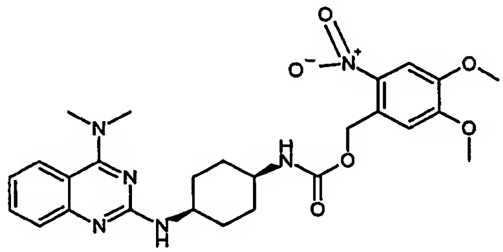
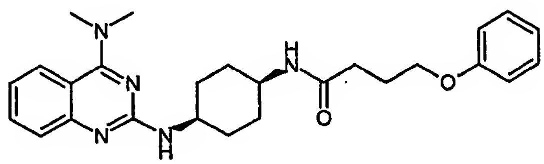
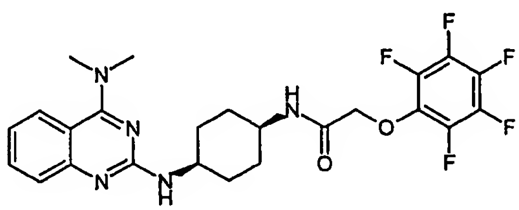
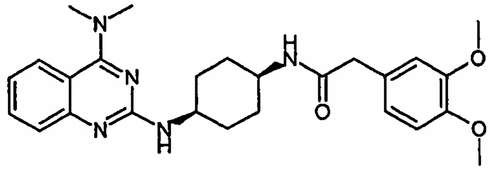
Example No.	Structure	APCI-MS
387		473 (M + H)
388		428 (M + H)
389		450 (M + H)
390		502 (M + H)
391		508 (M + H)

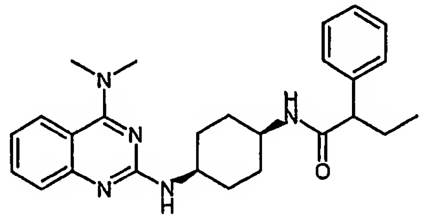
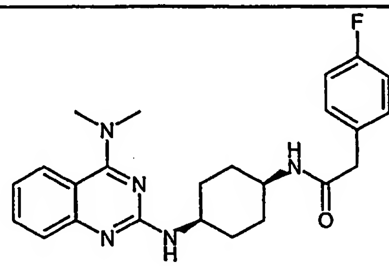
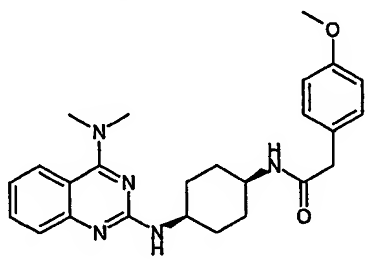
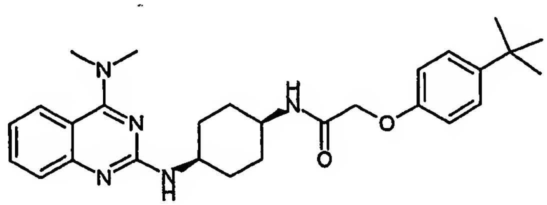
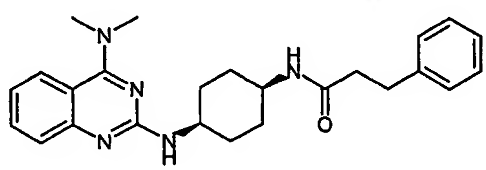
Example No.	Structure	APCI-MS
392		472 (M + H)
393		476 (M + H)
394		479 (M + H)
395		446 (M + H)
396		462 (M + H)

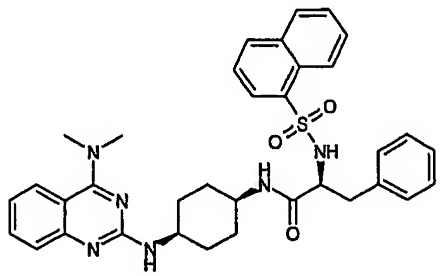
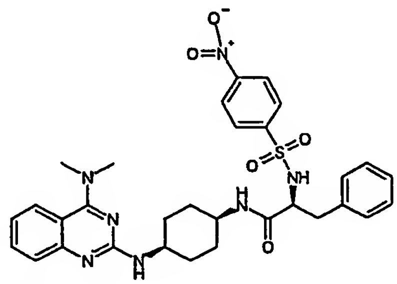
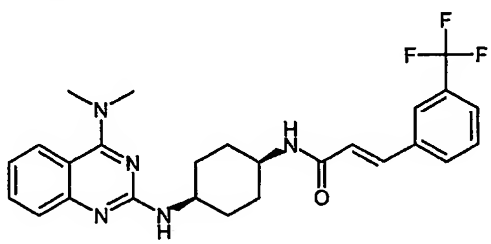
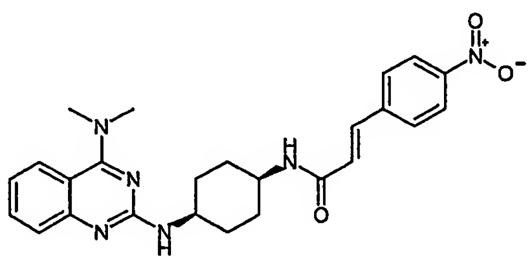
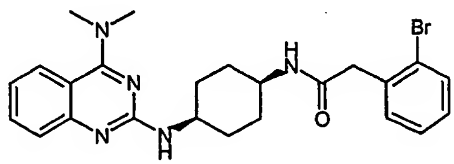
Example No.	Structure	APCI-MS
397		510 (M + H)
398		454 (M + H)
399		416 (M + H)
400		438 (M + H)
401		492 (M + H)

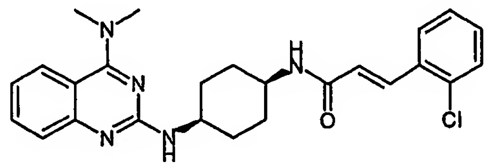
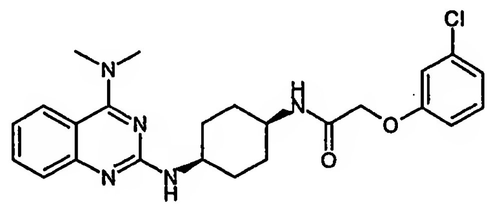
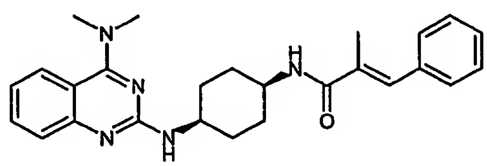
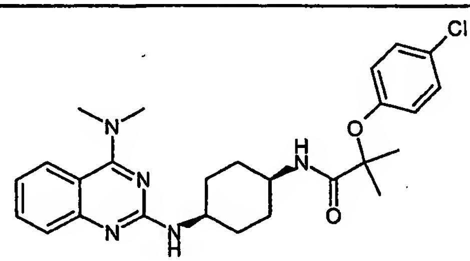
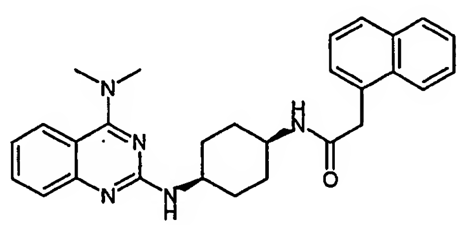
Example No.	Structure	APCI-MS
402		457 (M + H)
403		420 (M + H)
404		404 (M + H)
405		430 (M + H)
406		448 (M + H)

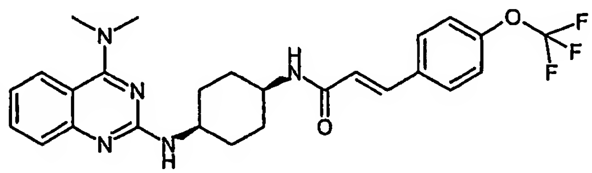
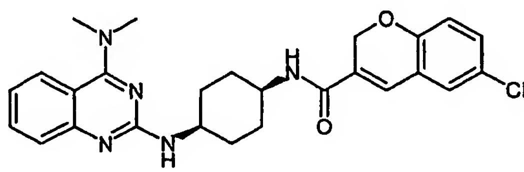
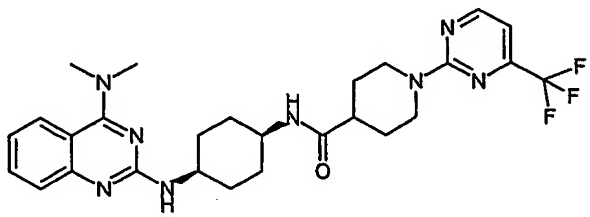
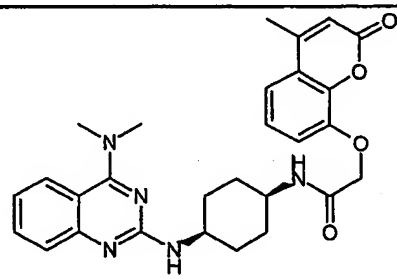
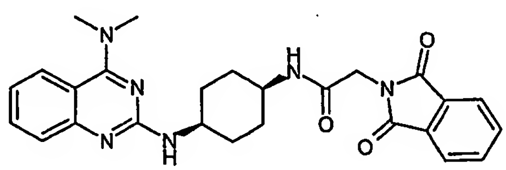
Example No.	Structure	APCI-MS
407		465 (M + H)
408		434 (M + H)
409		410 (M + H)
410		587 (M + H)
411		420 (M + H)

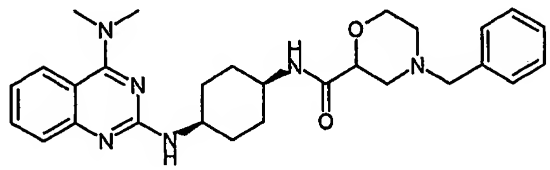
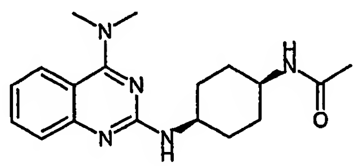
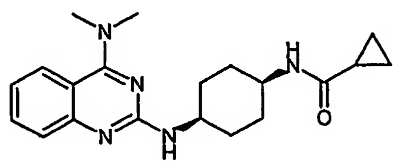
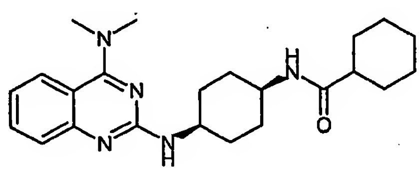
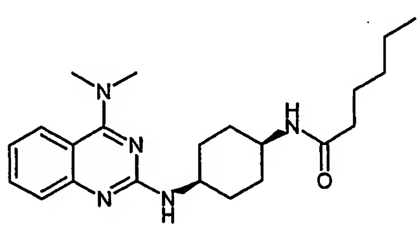
Example No.	Structure	APCI-MS
412		465 (M + H)
413		525 (M + H)
414		448 (M + H)
415		510 (M + H)
416		464 (M + H)

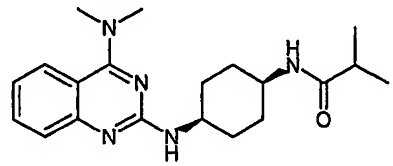
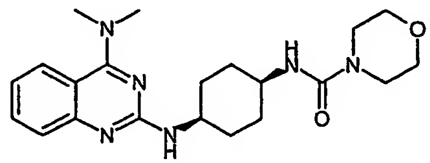
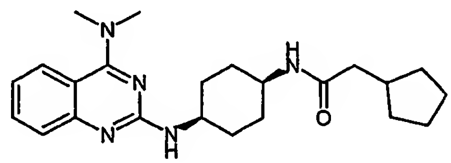
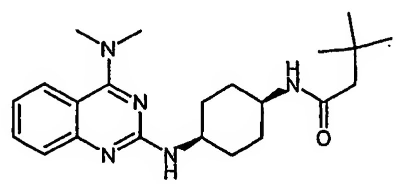
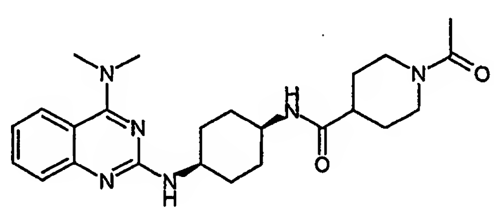
Example No.	Structure	APCI-MS
417		432 (M + H)
418		422 (M + H)
419		434 (M + H)
420		476 (M + H)
421		418 (M + H)

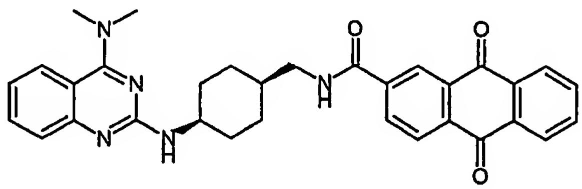
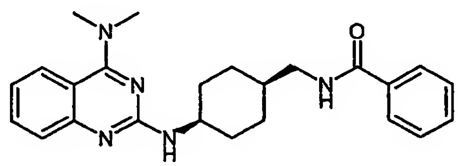
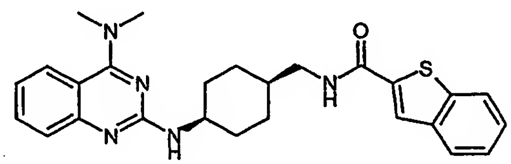
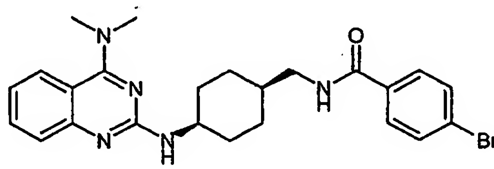
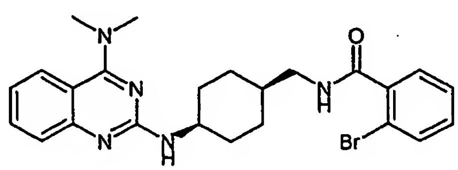
Example No.	Structure	APCI-MS
422		623 (M + H)
423		618 (M + H)
424		484 (M + H)
425		461 (M + H)
426		482 (M + H)

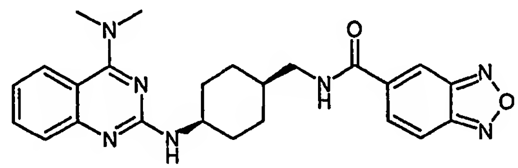
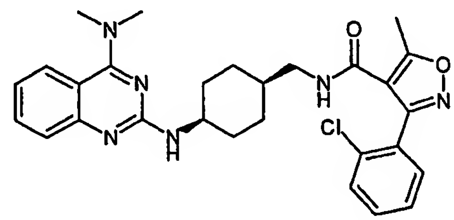
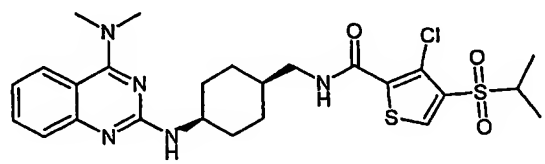
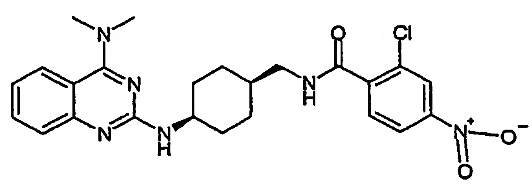
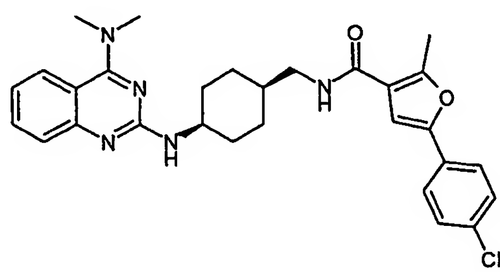
Example No.	Structure	APCI-MS
427		450 (M + H)
428		454 (M + H)
429		430 (M + H)
430		482 (M + H)
431		454 (M + H)

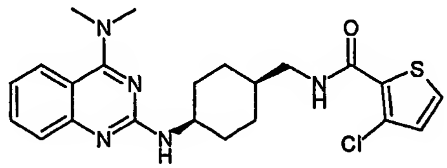
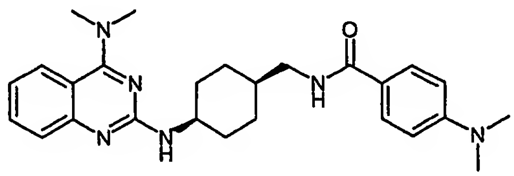
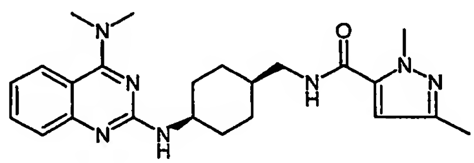
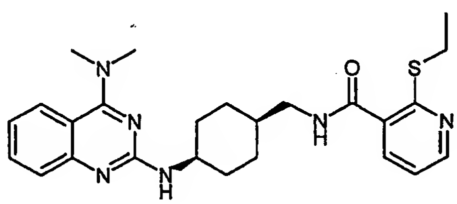
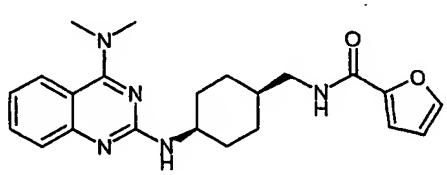
Example No.	Structure	APCI-MS
432		500 (M + H)
433		478 (M + H)
434		543 (M + H)
435		502 (M + H)
436		473 (M + H)

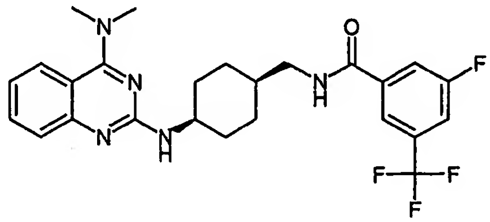
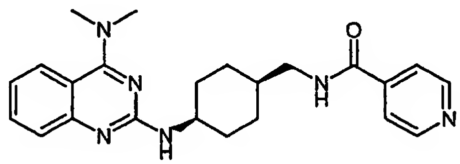
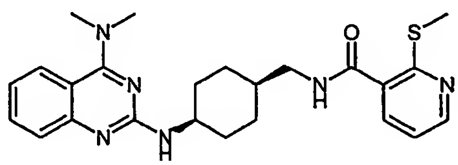
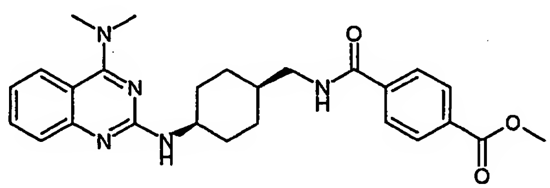
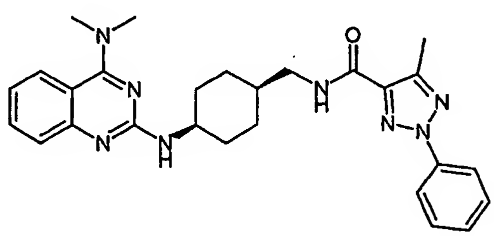
Example No.	Structure	APCI-MS
437		489 (M + H)
438		328 (M + H)
439		354 (M + H)
440		396 (M + H)
441		384 (M + H)

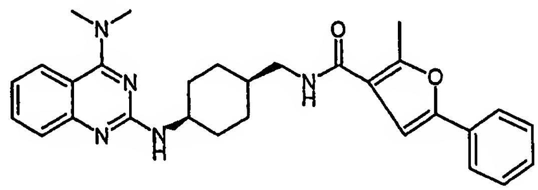
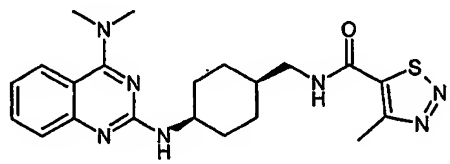
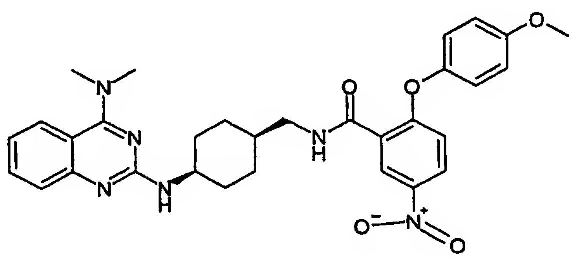
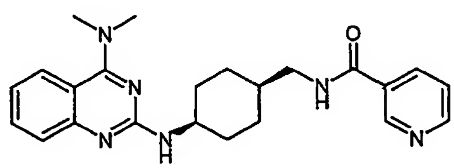
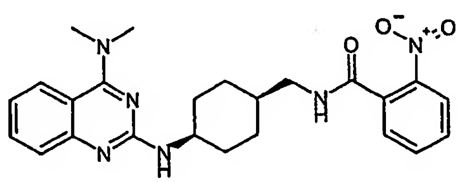
Example No.	Structure	APCI-MS
442		356 (M + H)
443		399 (M + H)
444		396 (M + H)
445		384 (M + H)
446		439 (M + H)

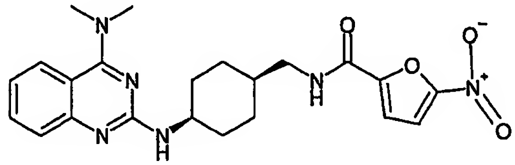
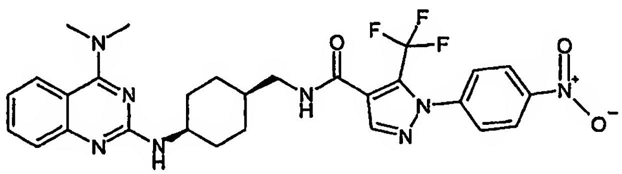
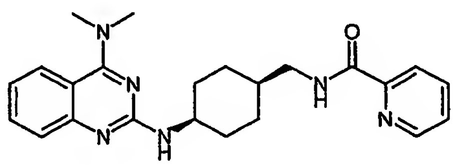
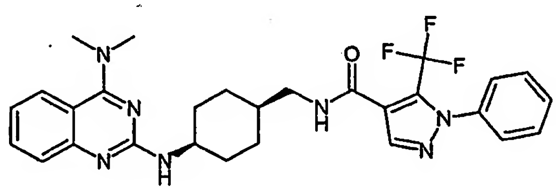
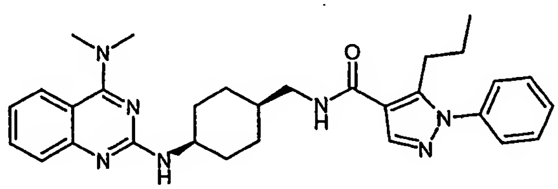
Example No.	Structure	APCI-MS
447		534 (M + H)
448		404 (M + H)
449		460 (M + H)
450		482 (M + H)
451		482 (M + H)

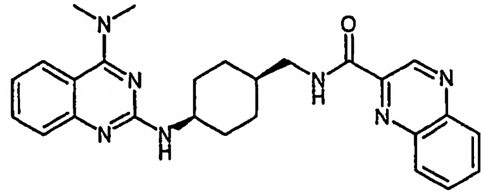
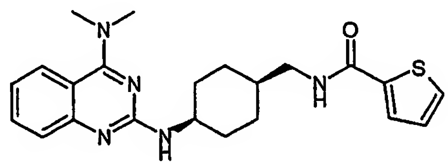
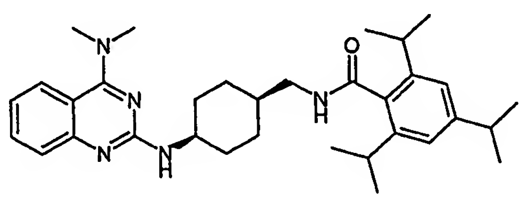
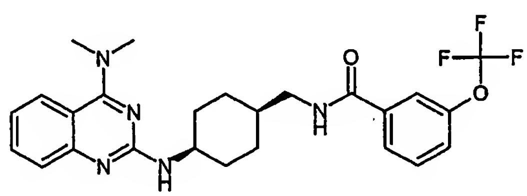
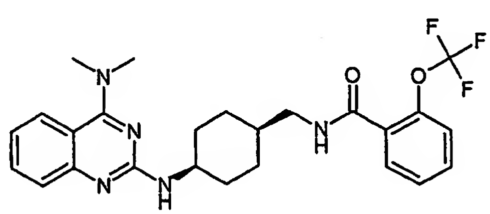
Example No.	Structure	APCI-MS
452		446 (M + H)
453		519 (M + H)
454		550 (M + H)
455		483 (M + H)
456		518 (M + H)

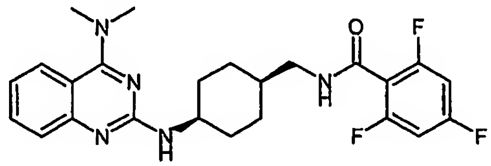
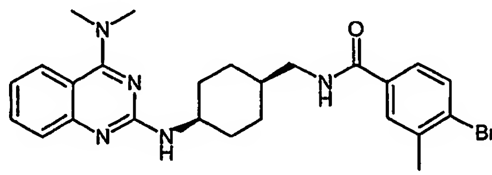
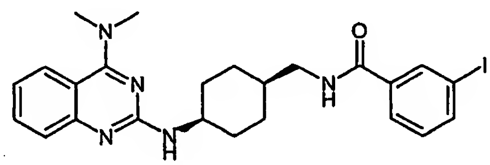
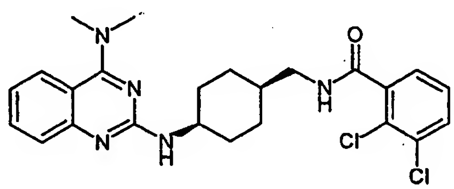
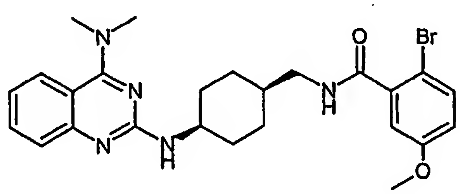
Example No.	Structure	APCI-MS
457		444 (M + H)
458		447 (M + H)
459		422 (M + H)
460		465 (M + H)
461		394 (M + H)

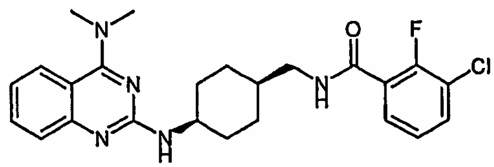
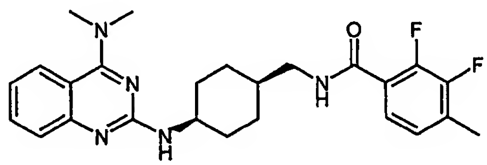
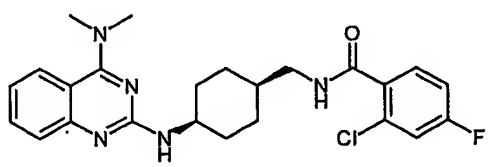
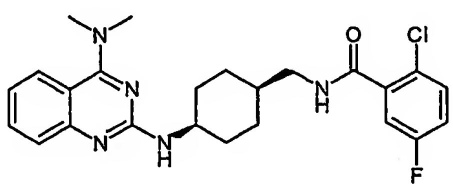
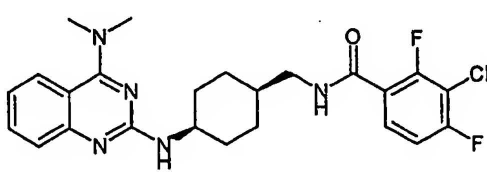
Example No.	Structure	APCI-MS
462		490 (M + H)
463		405 (M + H)
464		451 (M + H)
465		462 (M + H)
466		485 (M + H)

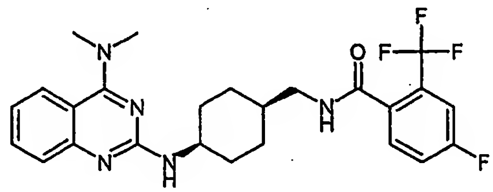
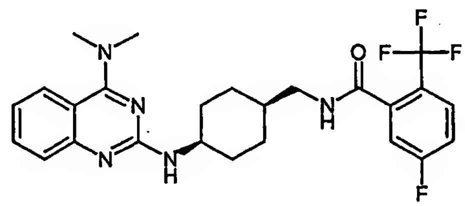
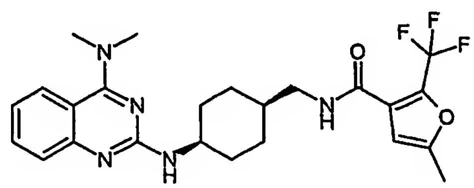
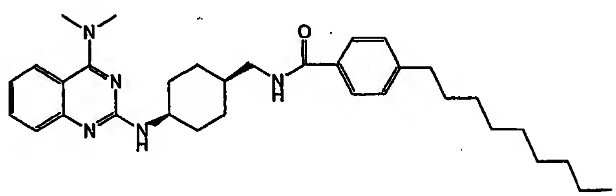
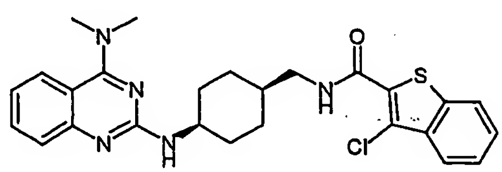
Example No.	Structure	APCI-MS
467		484 (M + H)
468		426 (M + H)
469		571 (M + H)
470		405 (M + H)
471		449 (M + H)

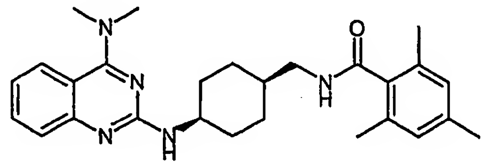
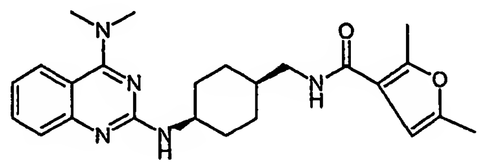
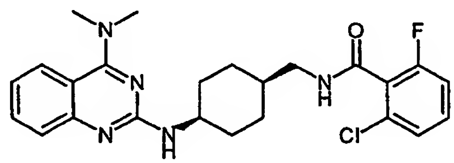
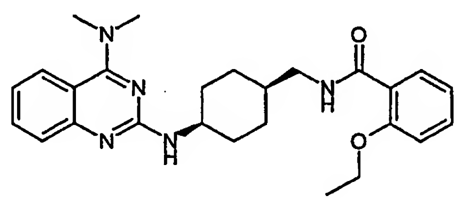
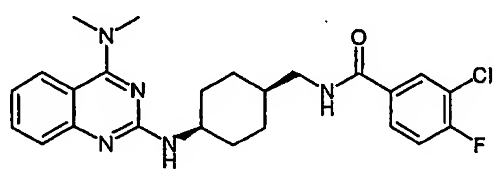
Example No.	Structure	APCI-MS
472		439 (M + H)
473		583 (M + H)
474		405 (M + H)
475		538 (M + H)
476		512 (M + H)

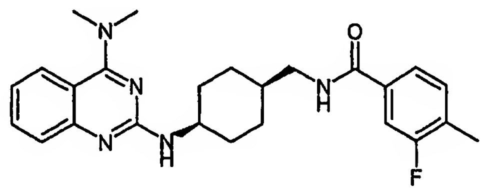
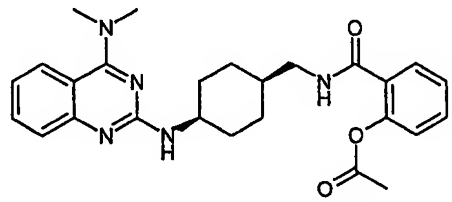
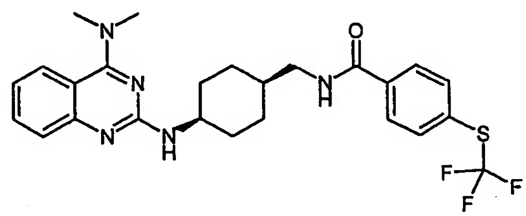
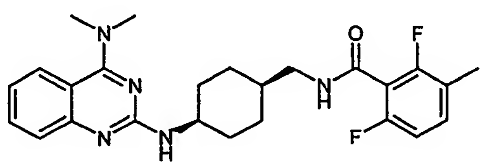
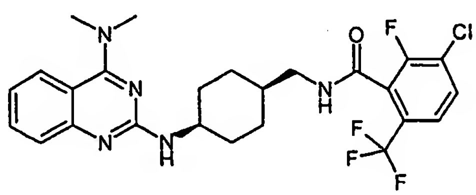
Example No.	Structure	APCI-MS
477		456 (M + H)
478		410 (M + H)
479		530 (M + H)
480		488 (M + H)
481		488 (M + H)

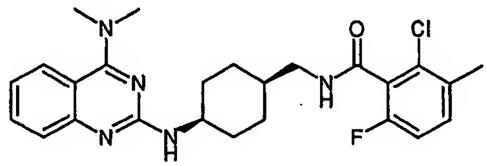
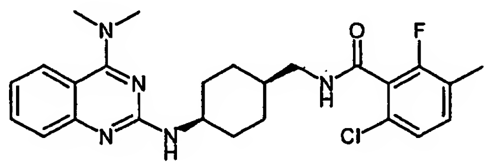
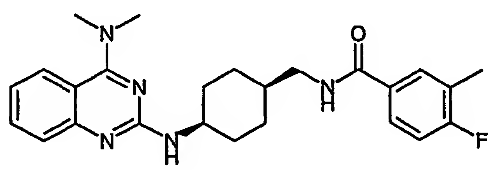
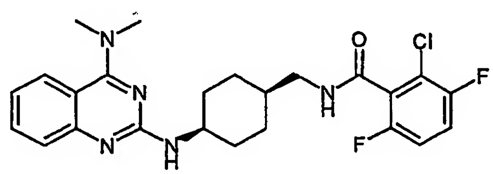
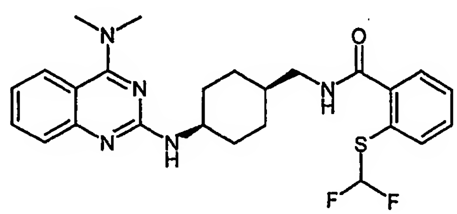
Example No.	Structure	APCI-MS
482		458 (M + H)
483		496 (M + H)
484		530 (M + H)
485		472 (M + H)
486		512 (M + H)

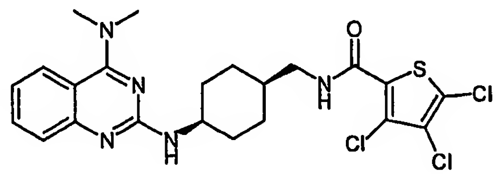
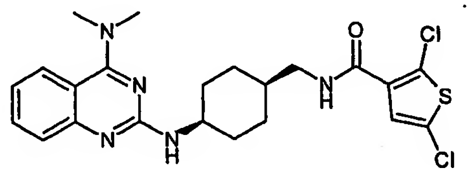
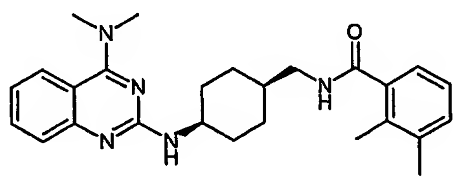
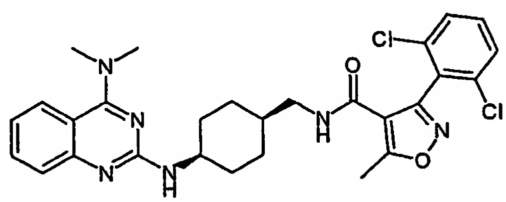
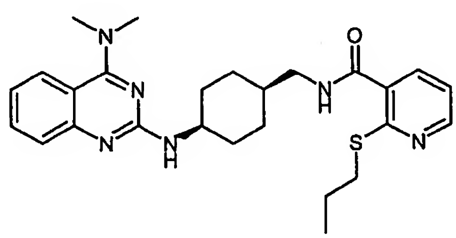
Example No.	Structure	APCI-MS
487		456 (M + H)
488		454 (M + H)
489		456 (M + H)
490		456 (M + H)
491		474 (M + H)

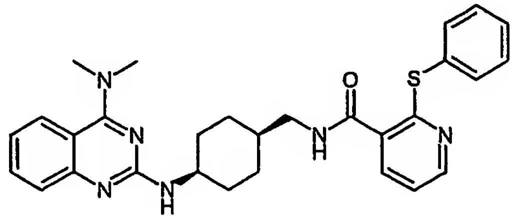
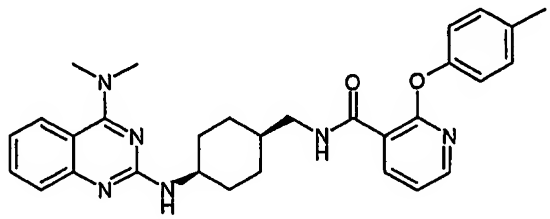
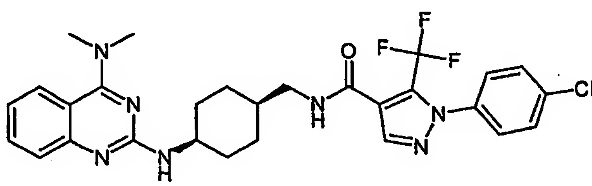
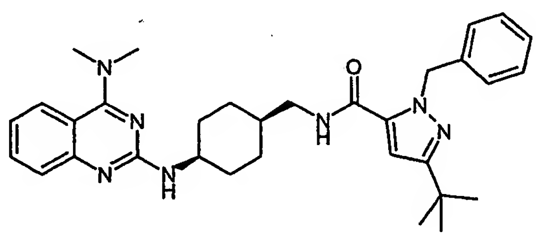
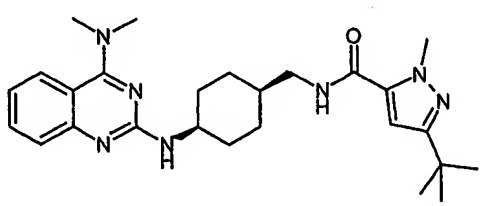
Example No.	Structure	APCI-MS
492		490 (M + H)
493		490 (M + H)
494		476 (M + H)
495		530 (M + H)
496		494 (M + H)

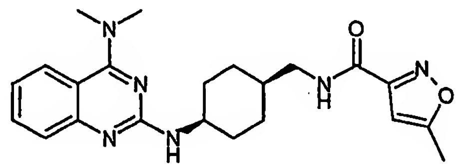
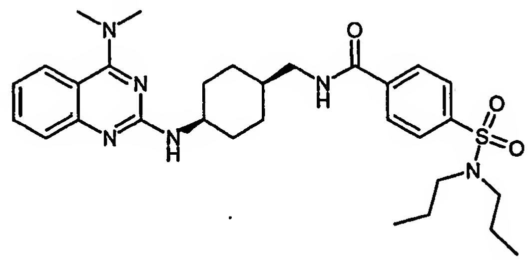
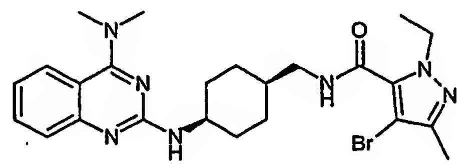
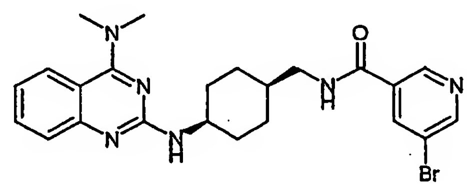
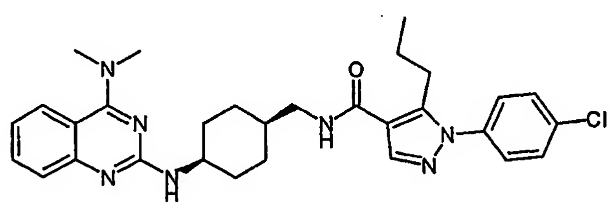
Example No.	Structure	APCI-MS
497		446 (M + H)
498		422 (M + H)
499		456 (M + H)
500		448 (M + H)
501		456 (M + H)

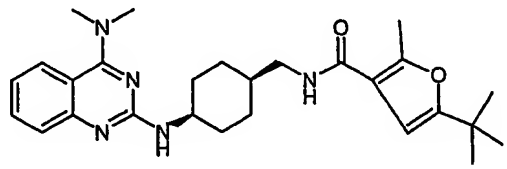
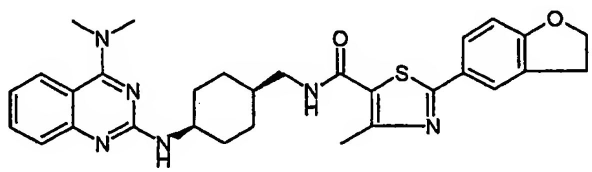
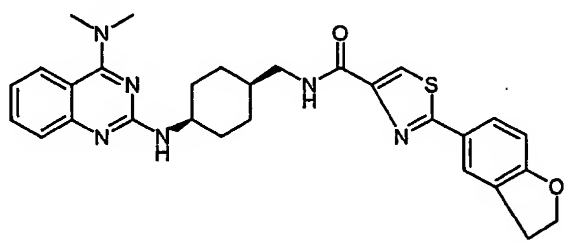
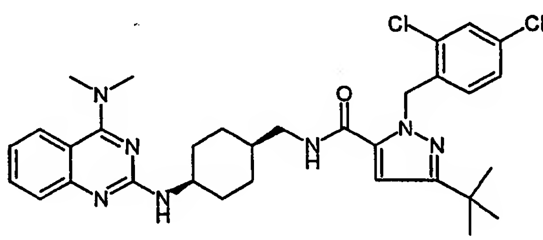
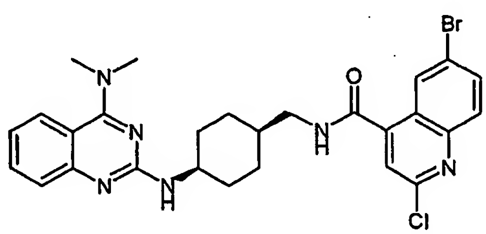
Example No.	Structure	APCI-MS
502		436 (M + H)
503		420 (M + H)
504		504 (M + H)
505		454 (M + H)
506		524 (M + H)

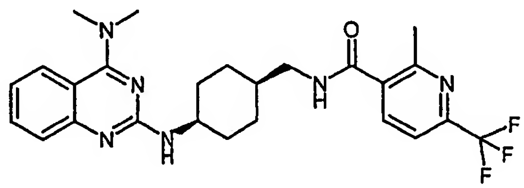
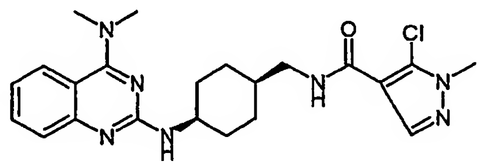
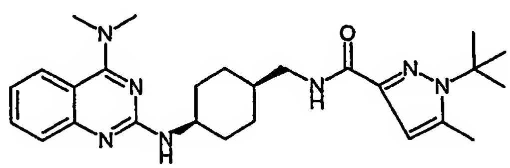
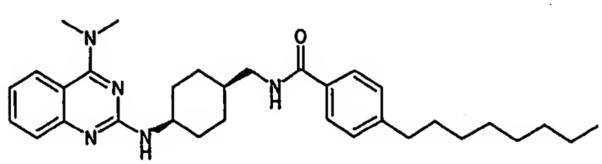
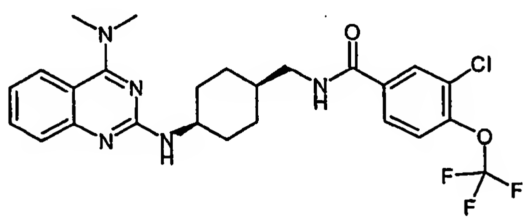
Example No.	Structure	APCI-MS
507		470 (M + H)
508		470 (M + H)
509		436 (M + H)
510		474 (M + H)
511		486 (M + H)

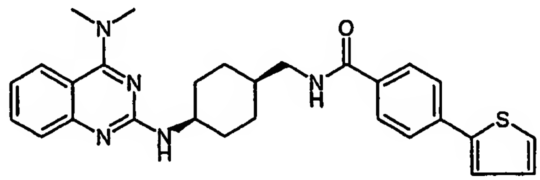
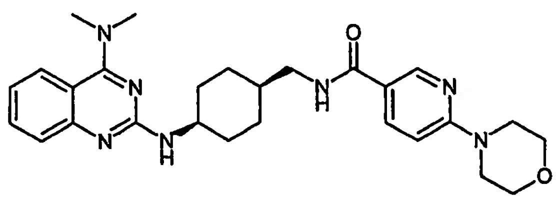
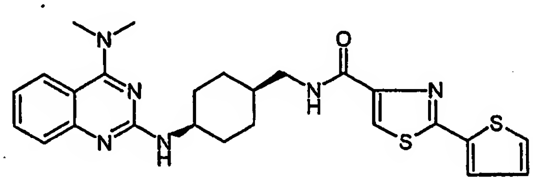
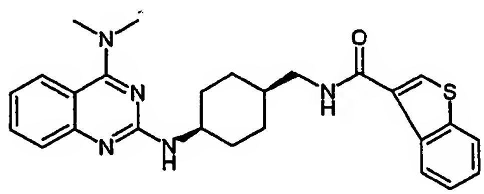
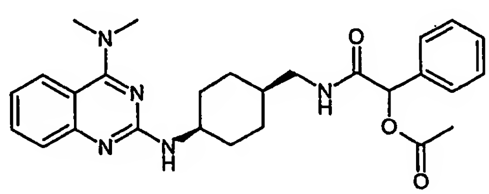
Example No.	Structure	APCI-MS
512		512 (M + H)
513		478 (M + H)
514		432 (M + H)
515		553 (M + H)
516		479 (M + H)

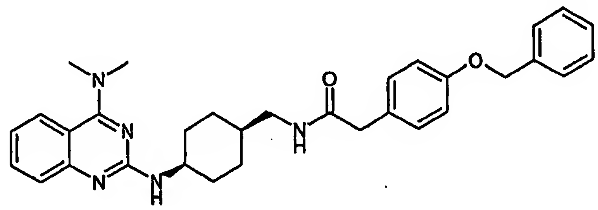
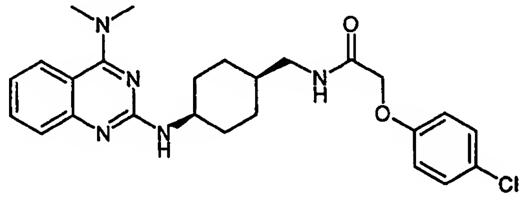
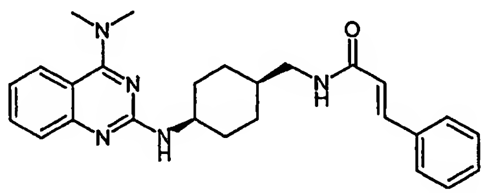
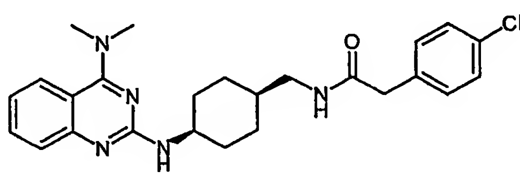
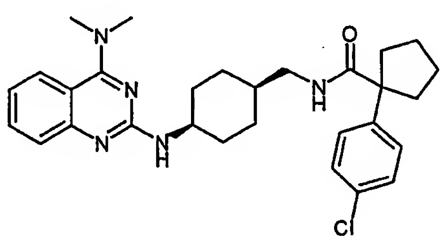
Example No.	Structure	APCI-MS
517		513 (M + H)
518		511 (M + H)
519		572 (M + H)
520		540 (M + H)
521		464 (M + H)

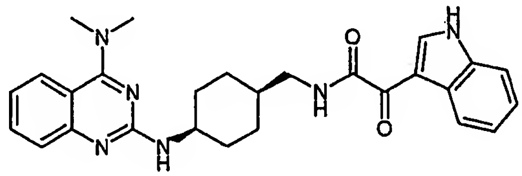
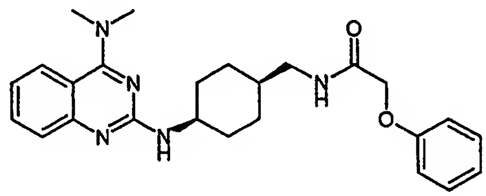
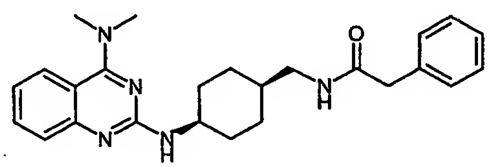
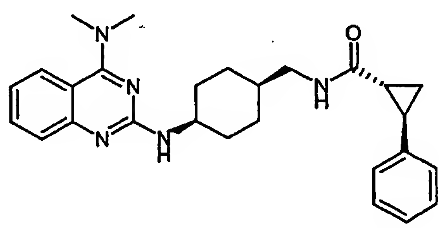
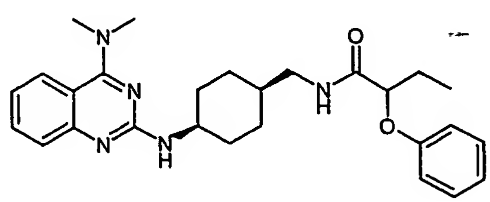
Example No.	Structure	APCI-MS
522		409 (M + H)
523		567 (M + H)
524		514 (M + H)
525		483 (M + H)
526		546 (M + H)

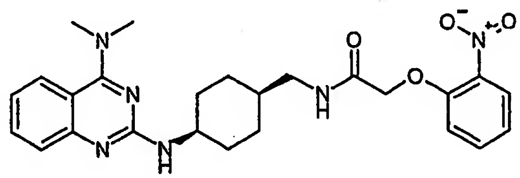
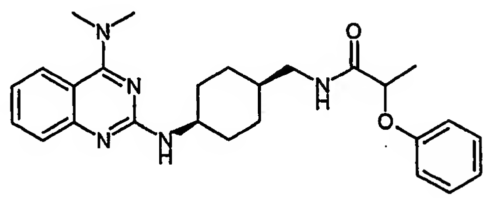
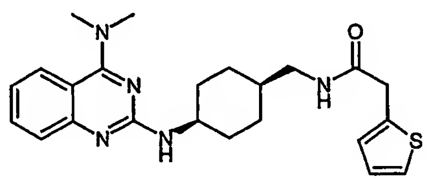
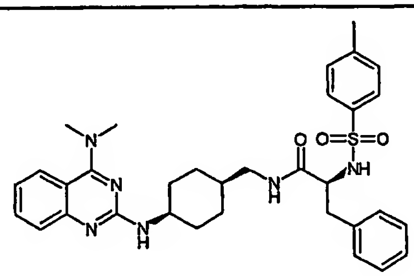
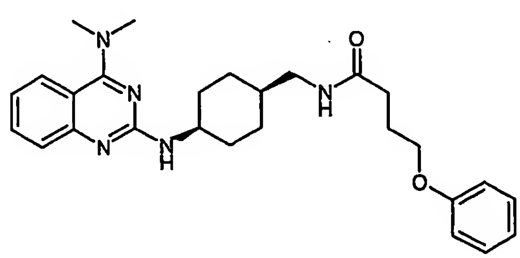
Example No.	Structure	APCI-MS
527		464 (M + H)
528		543 (M + H)
529		529 (M + H)
530		608 (M + H)
531		567 (M + H)

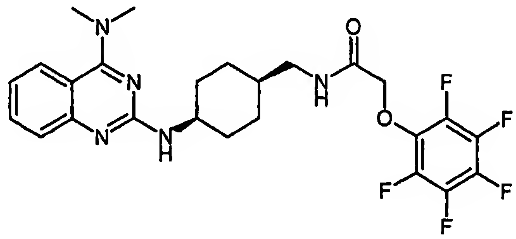
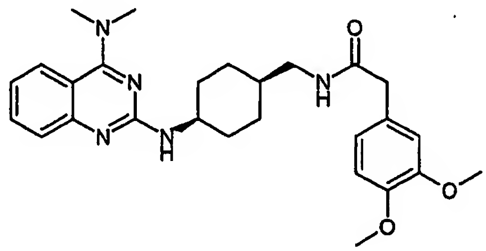
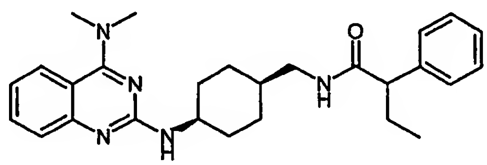
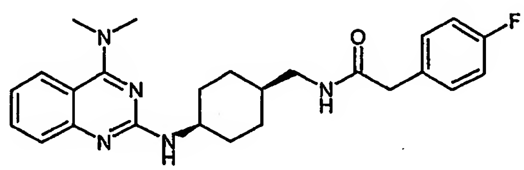
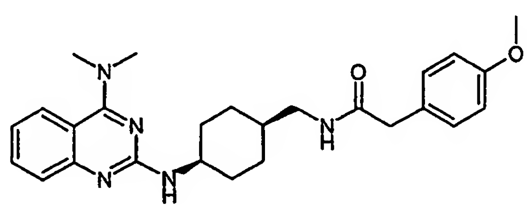
Example No.	Structure	APCI-MS
532		487 (M + H)
533		442 (M + H)
534		464 (M + H)
535		516 (M + H)
536		522 (M + H)

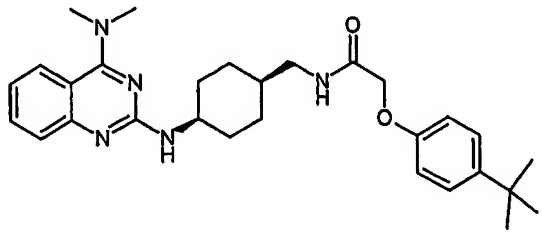
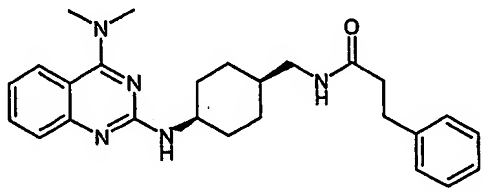
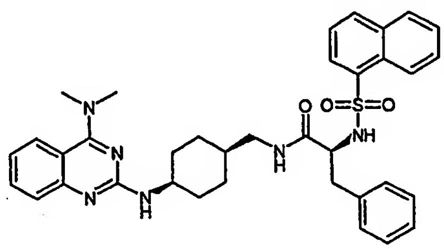
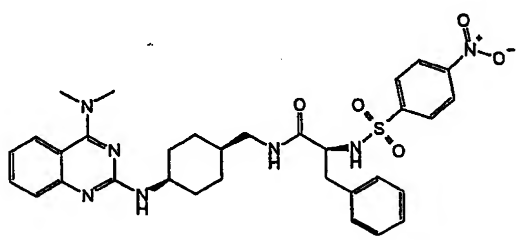
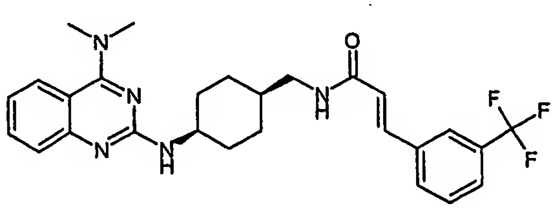
Example No.	Structure	APCI-MS
537		486 (M + H)
538		490 (M + H)
539		493 (M + H)
540		460 (M + H)
541		476 (M + H)

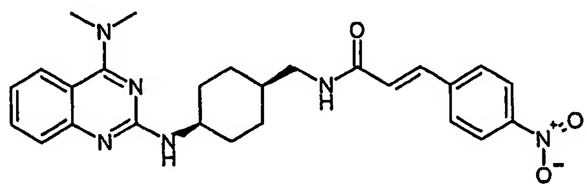
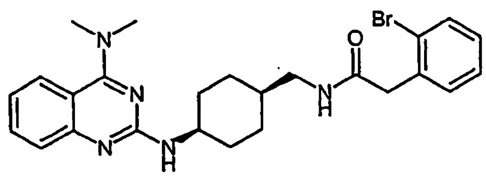
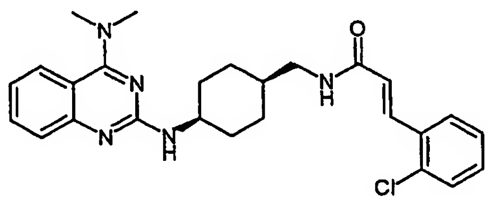
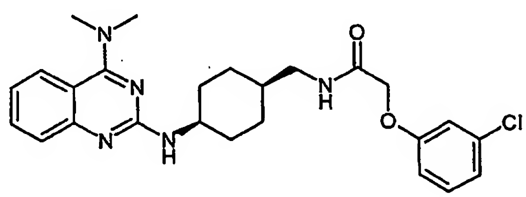
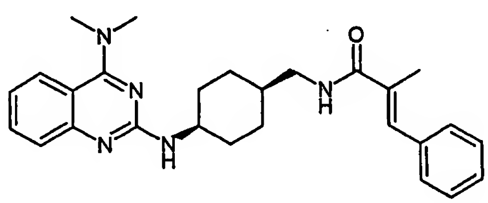
Example No.	Structure	APCI-MS
542		524 (M + H)
543		468 (M + H)
544		430 (M + H)
545		452 (M + H)
546		506 (M + H)

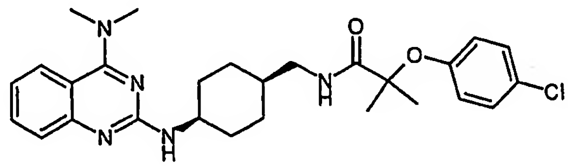
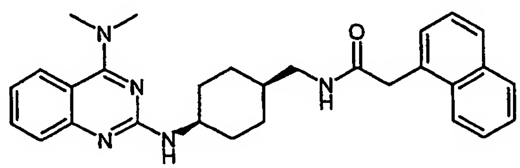
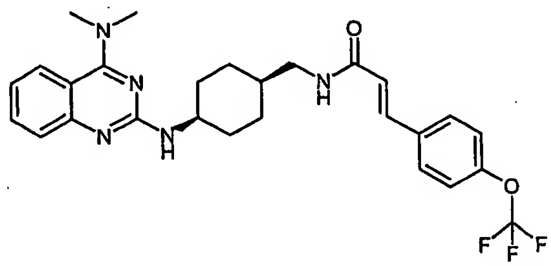
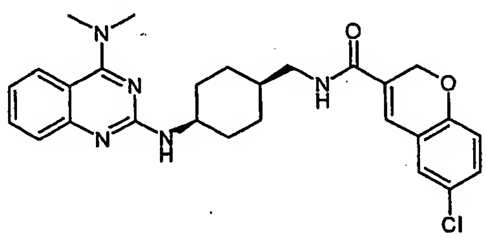
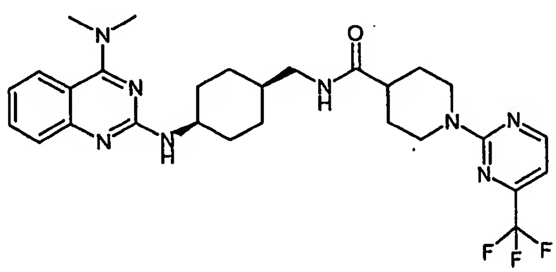
Example No.	Structure	APCI-MS
547		471 (M + H)
548		434 (M + H)
549		418 (M + H)
550		444 (M + H)
551		462 (M + H)

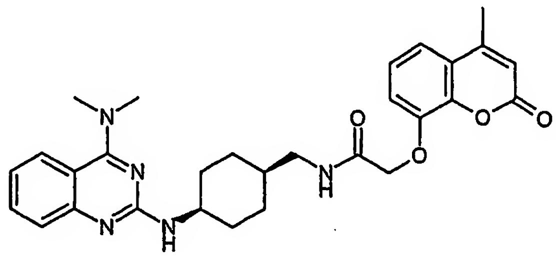
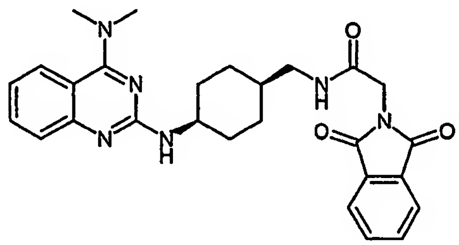
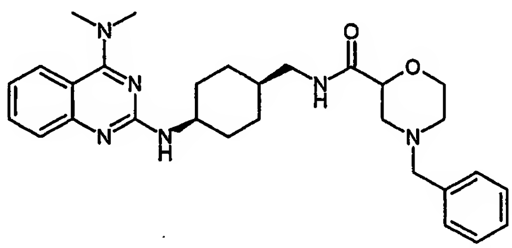
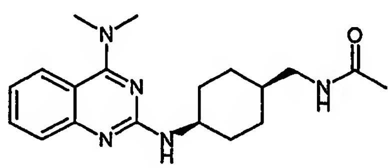
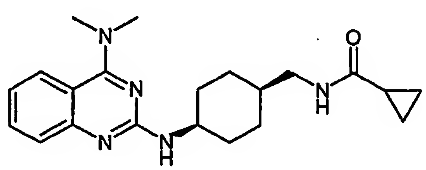
Example No.	Structure	APCI-MS
552		479 (M + H)
553		448 (M + H)
554		424 (M + H)
555		601 (M + H)
556		462 (M + H)

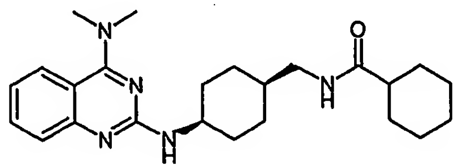
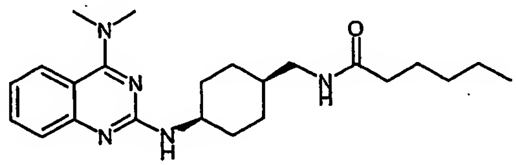
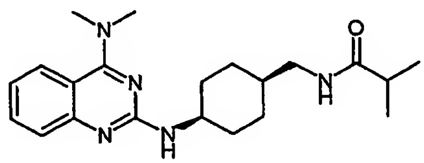
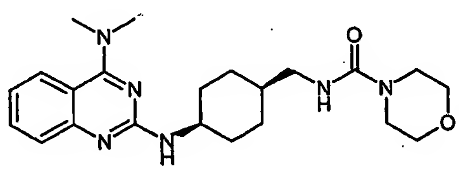
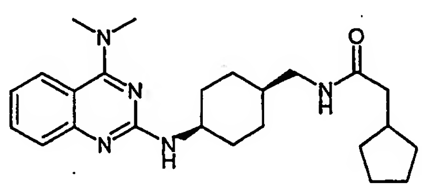
Example No.	Structure	APCI-MS
557		524 (M + H)
558		478 (M + H)
559		446 (M + H)
560		436 (M + H)
561		448 (M + H)

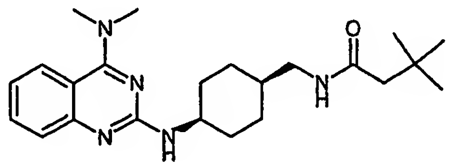
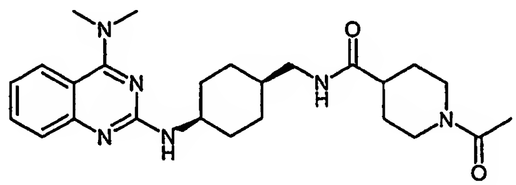
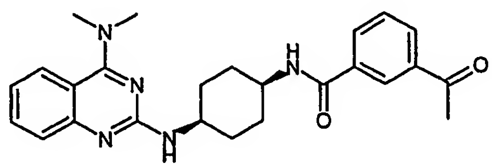
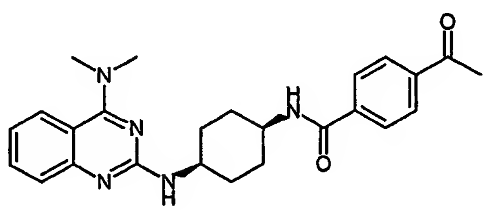
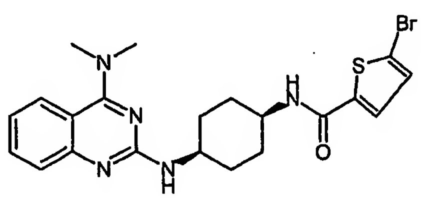
Example No.	Structure	APCI-MS
562		490 (M + H)
563		432 (M + H)
564		637 (M + H)
565		632 (M + H)
566		498 (M + H)

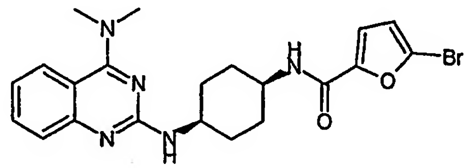
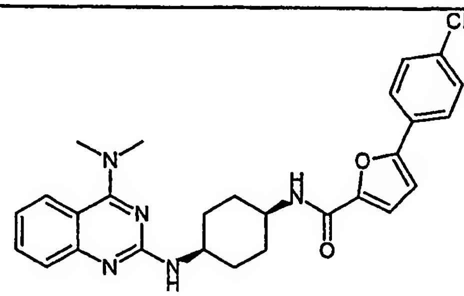
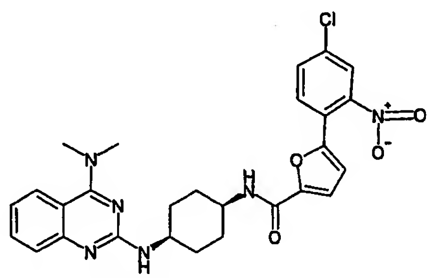
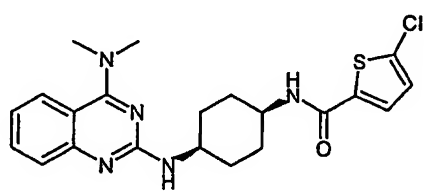
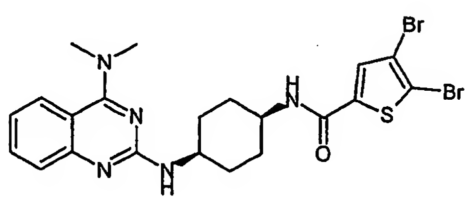
Example No.	Structure	APCI-MS
567		475 (M + H)
568		496 (M + H)
569		464 (M + H)
570		468 (M + H)
571		444 (M + H)

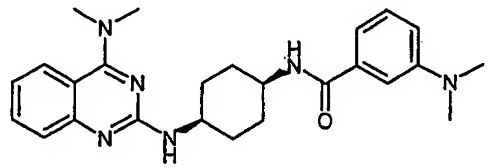
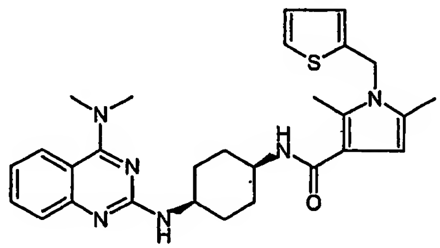
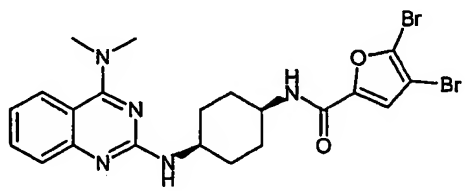
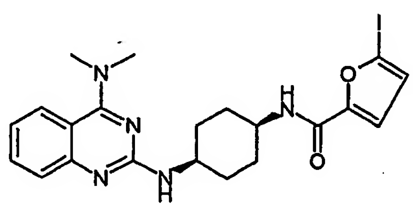
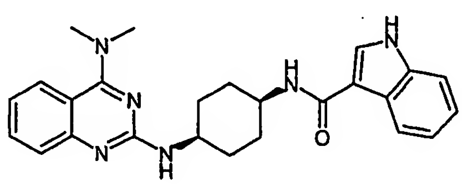
Example No.	Structure	APCI-MS
572		496 (M + H)
573		468 (M + H)
574		514 (M + H)
575		492 (M + H)
576		557 (M + H)

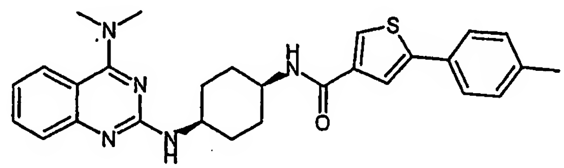
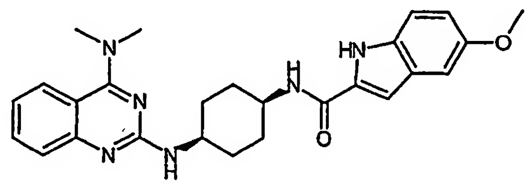
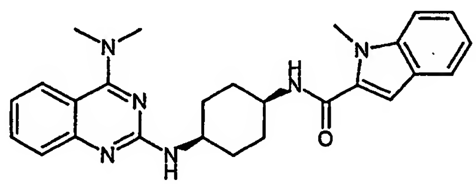
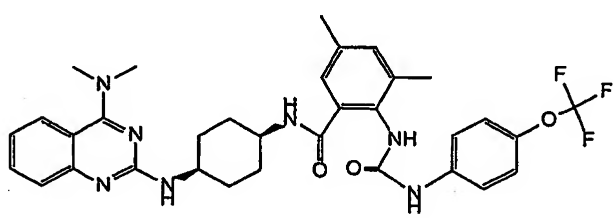
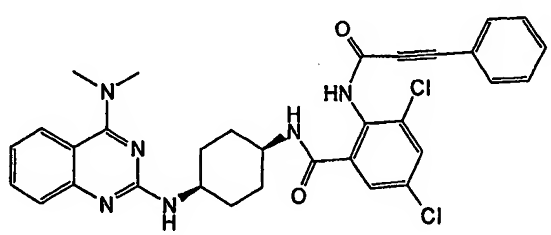
Example No.	Structure	APCI-MS
577		516 (M + H)
578		487 (M + H)
579		503 (M + H)
580		342 (M + H)
581		368 (M + H)

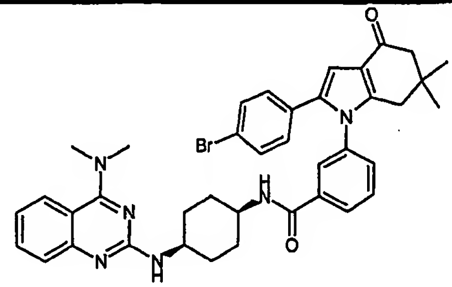
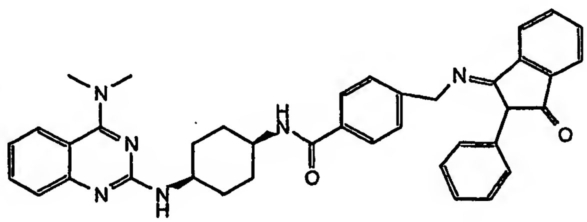
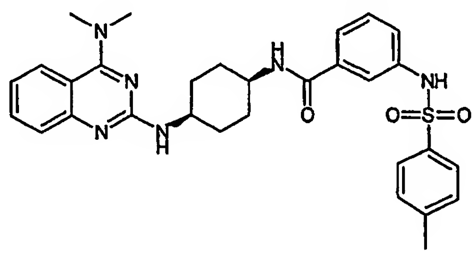
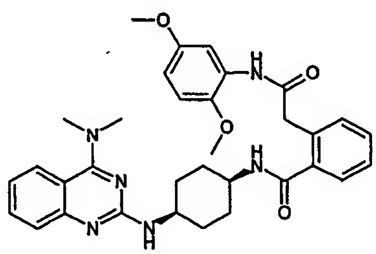
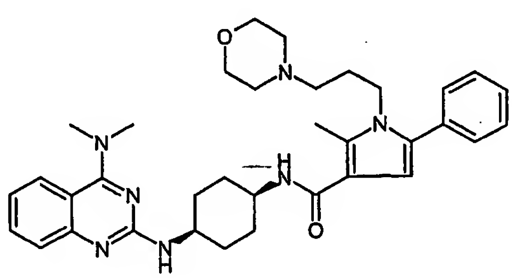
Example No.	Structure	APCI-MS
582		410 (M + H)
583		398 (M + H)
584		370 (M + H)
585		413 (M + H)
586		410 (M + H)

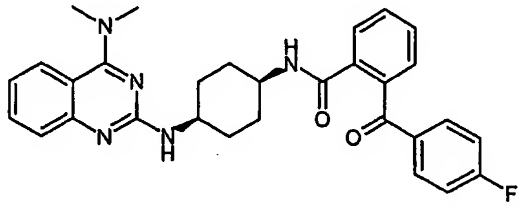
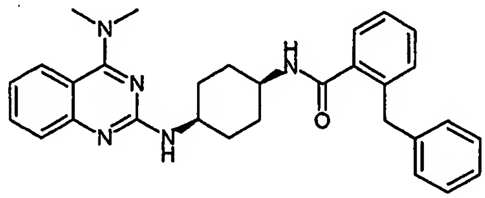
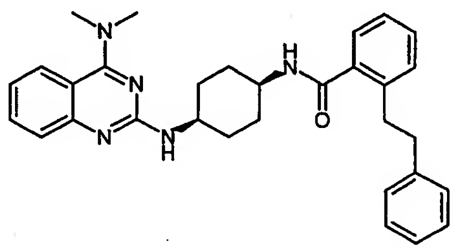
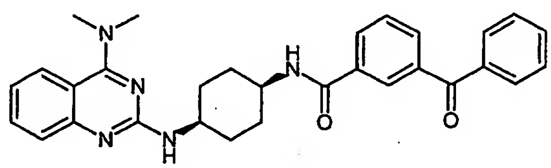
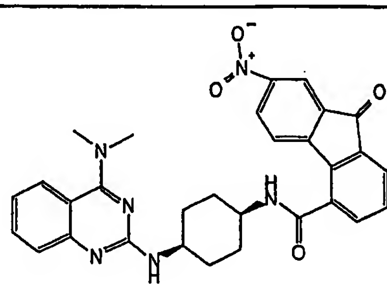
Example No.	Structure	APCI-MS
587		398 (M + H)
588		453 (M + H)
589		432 (M + H)
590		432 (M + H)
591		474 (M + H)

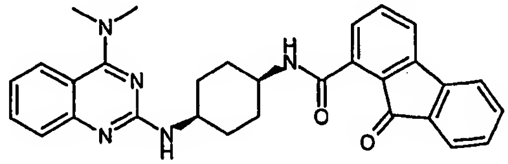
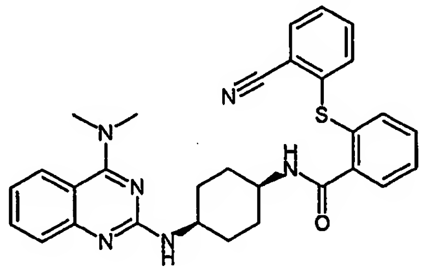
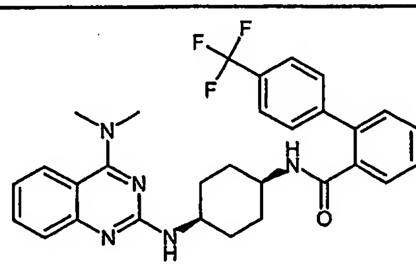
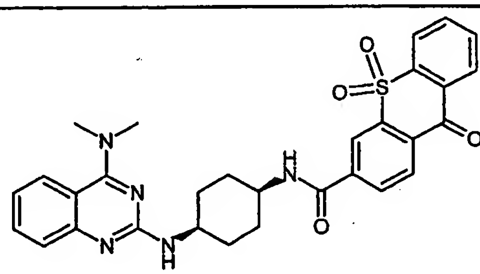
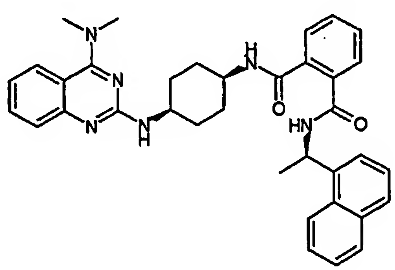
Example No.	Structure	APCI-MS
592		458 (M + H)
593		490 (M + H)
594		535 (M + H)
595		430 (M + H)
596		552 (M + H)

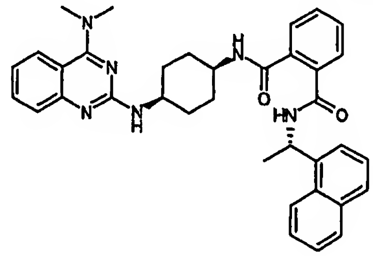
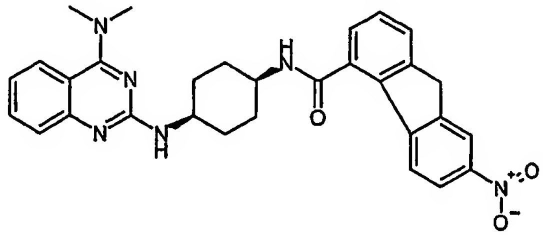
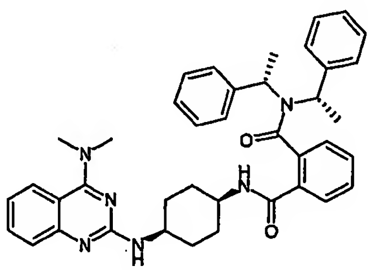
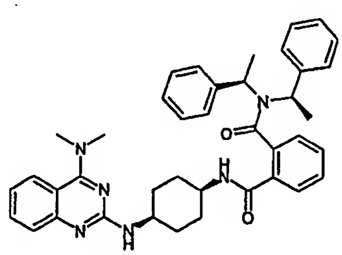
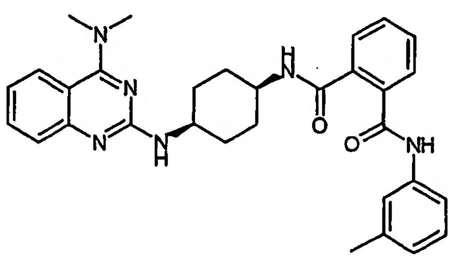
Example No.	Structure	APCI-MS
597		433 (M + H)
598		503 (M + H)
599		536 (M + H)
600		506 (M + H)
601		429 (M + H)

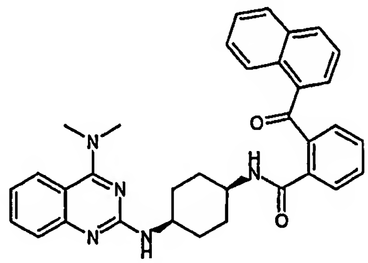
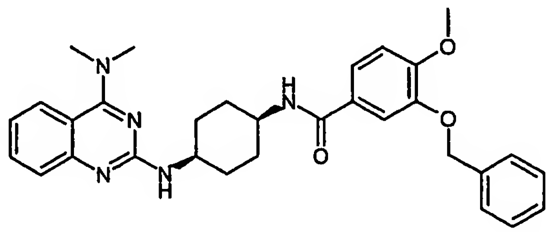
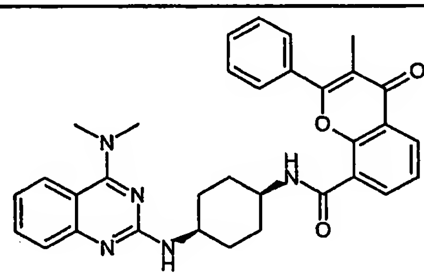
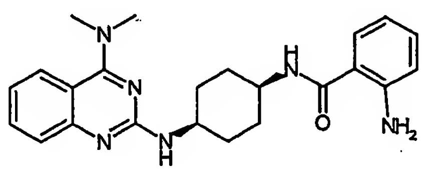
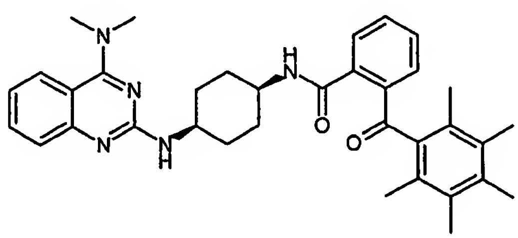
Example No.	Structure	APCI-MS
602		486 (M + H)
603		459 (M + H)
604		443 (M + H)
605		636 (M + H)
606		601 (M + H)

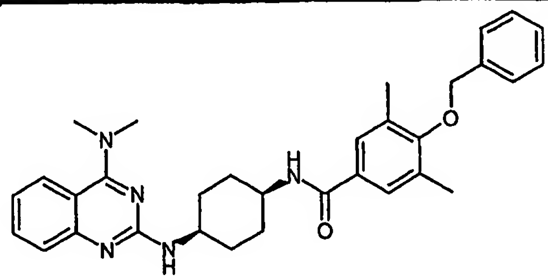
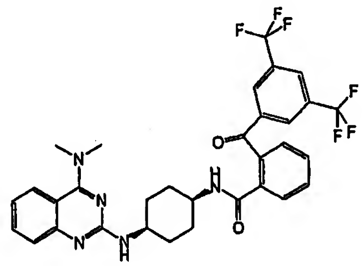
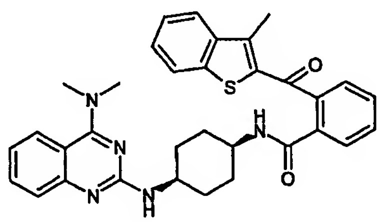
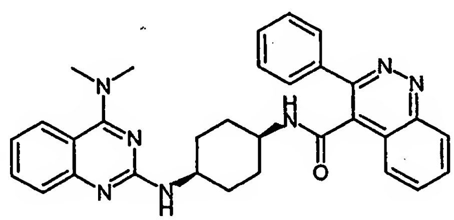
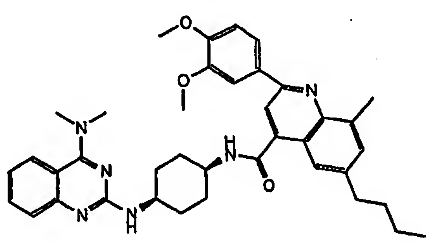
Example No.	Structure	APCI-MS
607		705 (M + H)
608		623 (M + H)
609		559 (M + H)
610		583 (M + H)
611		596 (M + H)

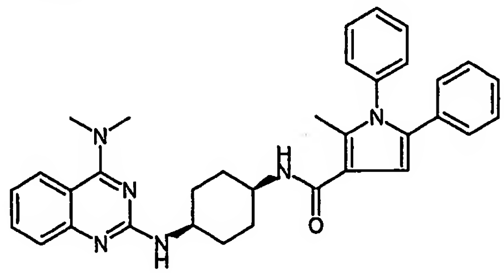
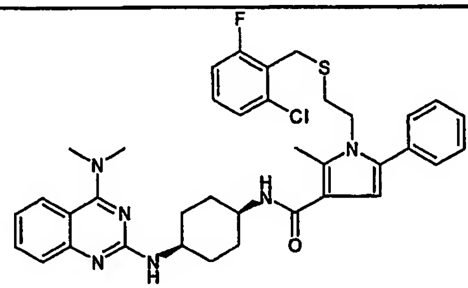
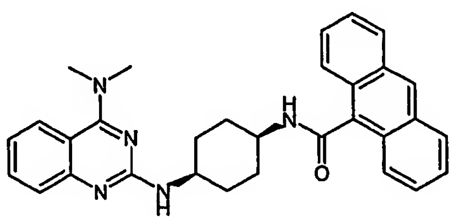
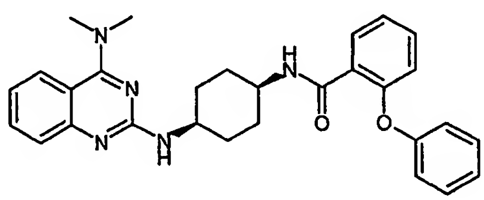
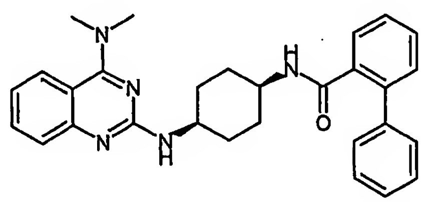
Example No.	Structure	APCI-MS
612		512 (M + H)
613		480 (M + H)
614		494 (M + H)
615		494 (M + H)
616		537 (M + H)

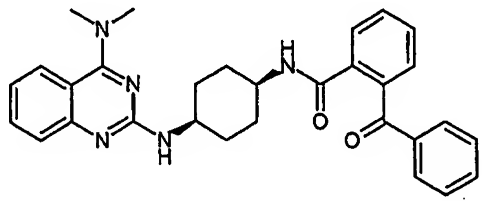
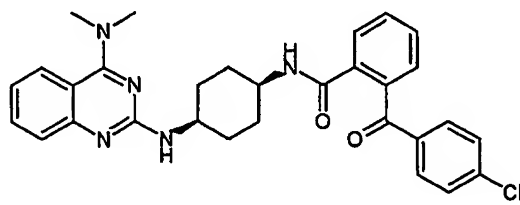
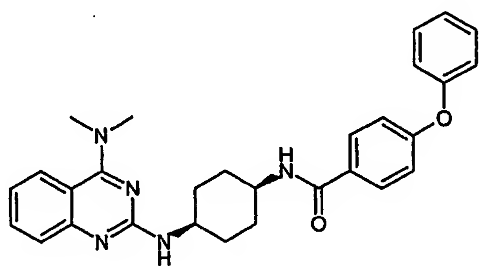
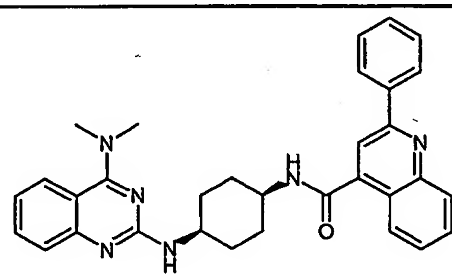
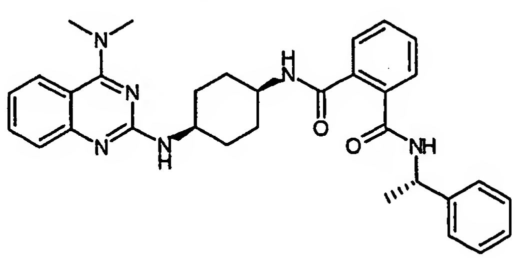
Example No.	Structure	APCI-MS
617		492 (M + H)
618		523 (M + H)
619		534 (M + H)
620		556 (M + H)
621		587 (M + H)

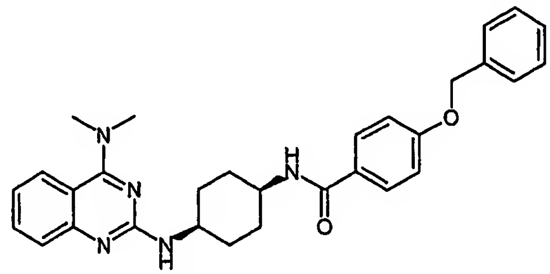
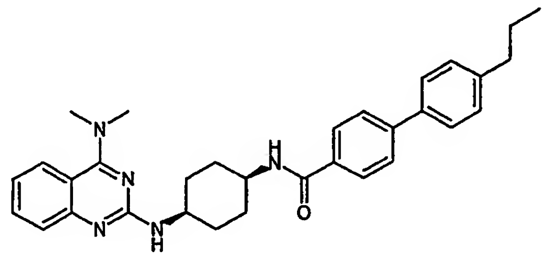
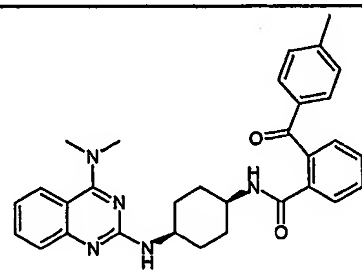
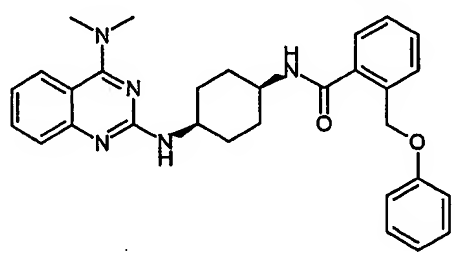
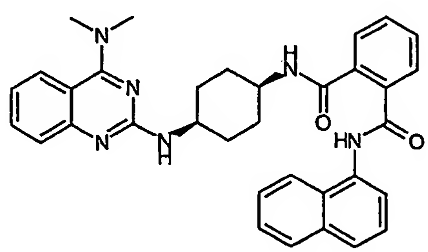
Example No.	Structure	APCI-MS
622		587 (M + H)
623		523 (M + H)
624		641 (M + H)
625		641 (M + H)
626		523 (M + H)

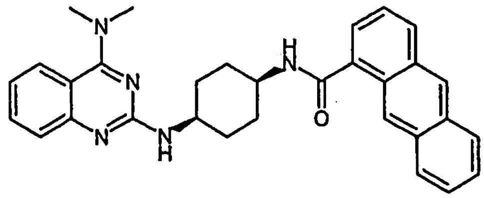
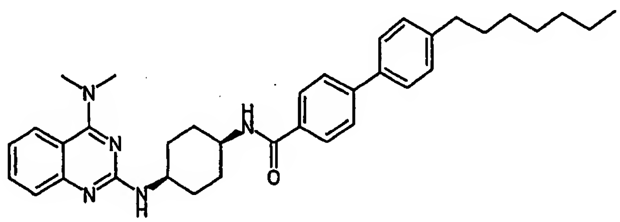
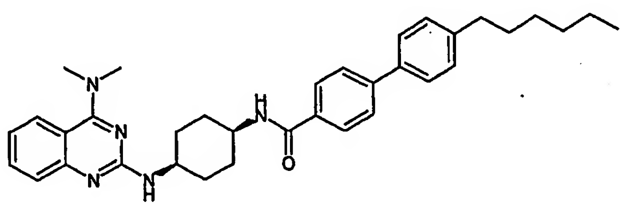
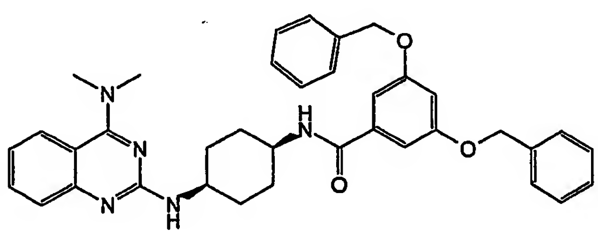
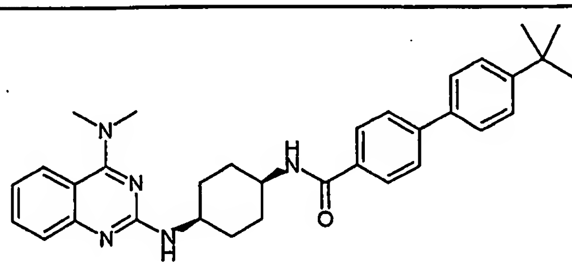
Example No.	Structure	APCI-MS
627		544 (M + H)
628		526 (M + H)
629		548 (M + H)
630		405 (M + H)
631		564 (M + H)

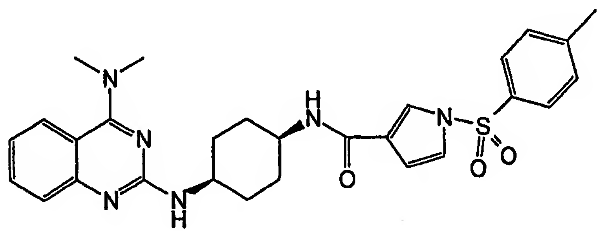
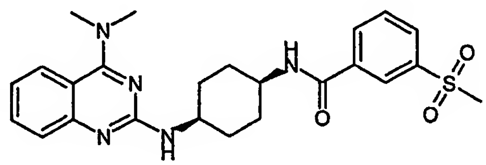
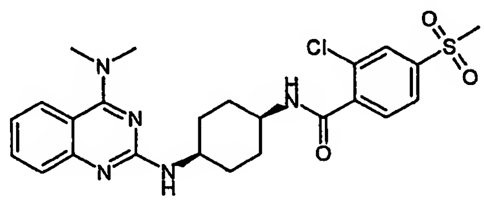
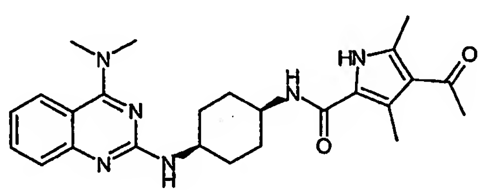
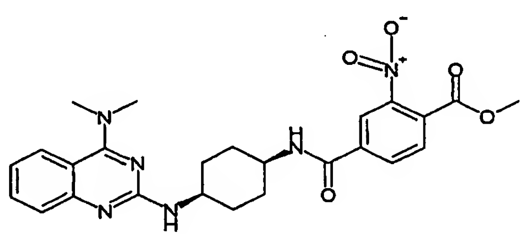
Example No.	Structure	APCI-MS
632		524 (M + H)
633		630 (M + H)
634		564 (M + H)
635		518 (M + H)
636		647 (M + H)

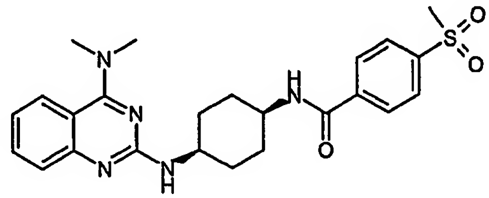
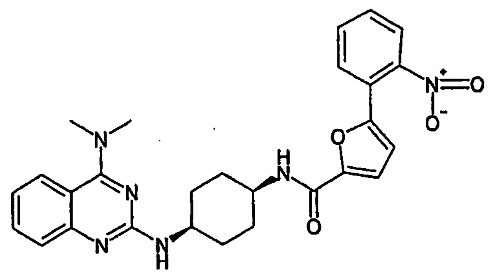
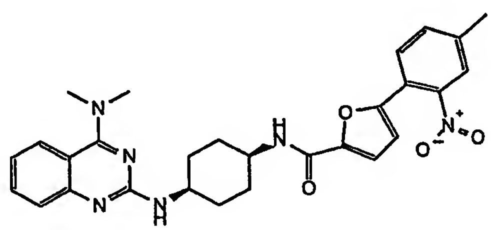
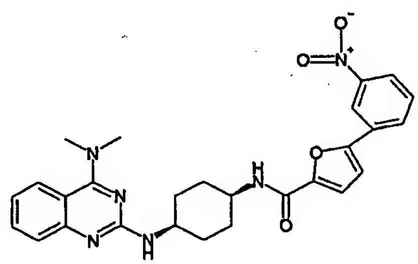
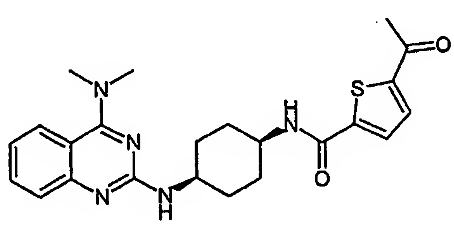
Example No.	Structure	APCI-MS
637		545 (M + H)
638		671 (M + H)
639		490 (M + H)
640		482 (M + H)
641		466 (M + H)

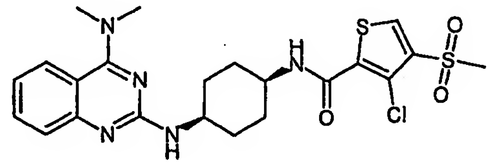
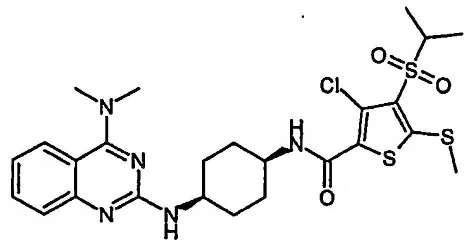
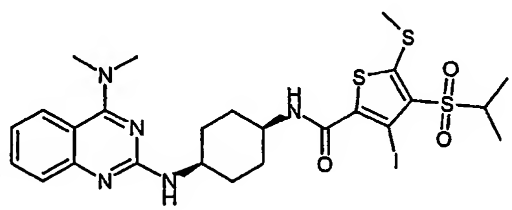
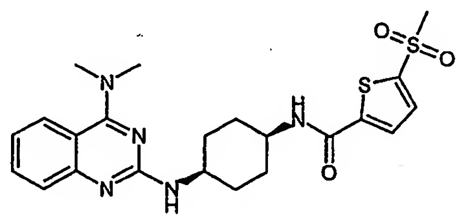
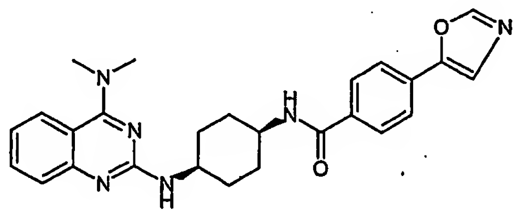
Example No.	Structure	APCI-MS
642		494 (M + H)
643		528 (M + H)
644		482 (M + H)
645		517 (M + H)
646		537 (M + H)

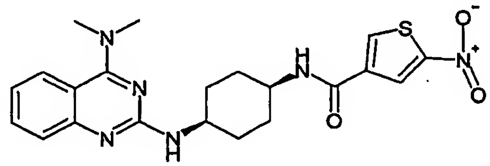
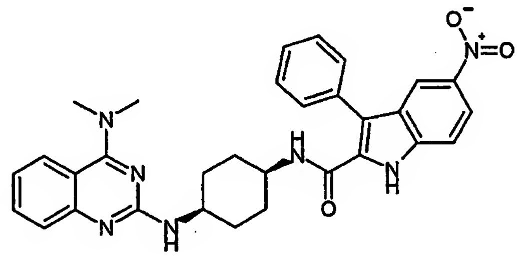
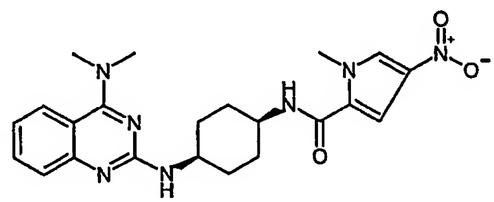
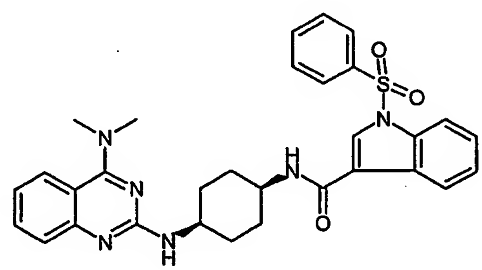
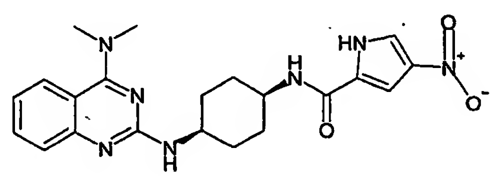
Example No.	Structure	APCI-MS
647		496 (M + H)
648		508 (M + H)
649		508 (M + H)
650		496 (M + H)
651		559 (M + H)

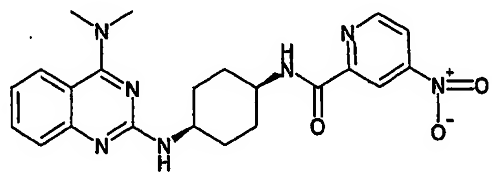
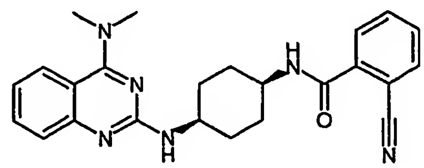
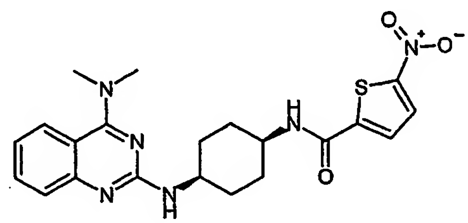
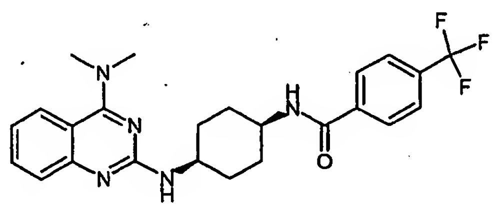
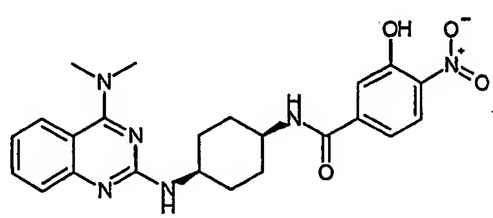
Example No.	Structure	APCI-MS
652		490 (M + H)
653		564 (M + H)
654		550 (M + H)
655		602 (M + H)
656		522 (M + H)

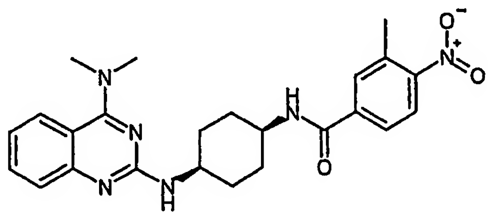
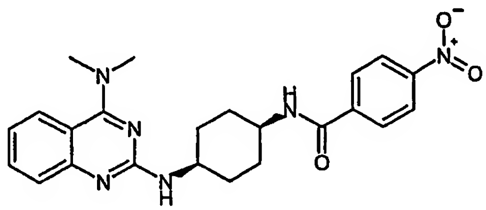
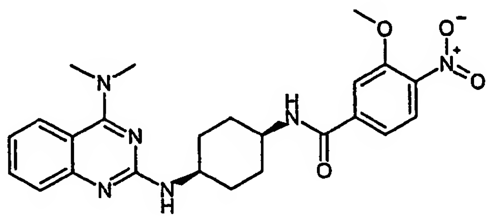
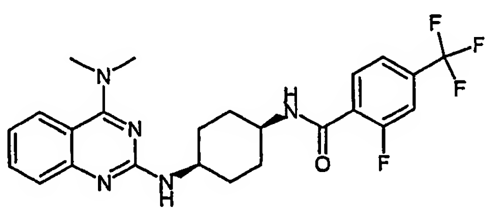
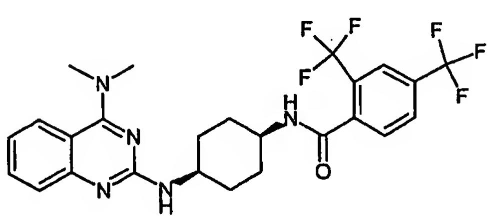
Example No.	Structure	APCI-MS
657		533 (M + H)
658		468 (M + H)
659		502 (M + H)
660		449 (M + H)
661		493 (M + H)

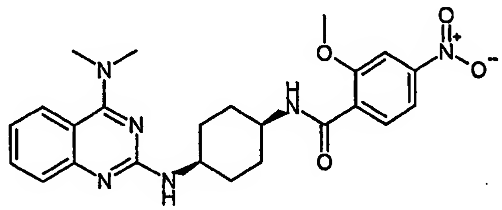
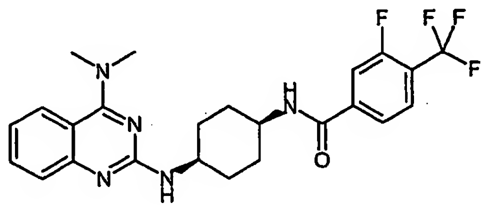
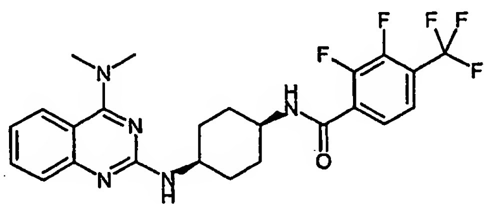
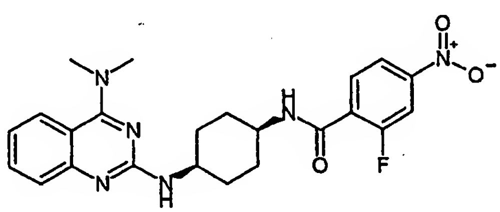
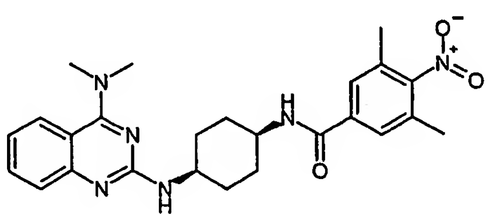
Example No.	Structure	APCI-MS
662		468 (M + H)
663		501 (M + H)
664		515 (M + H)
665		501 (M + H)
666		438 (M + H)

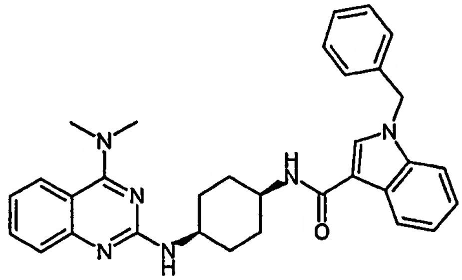
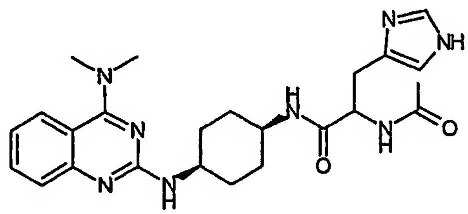
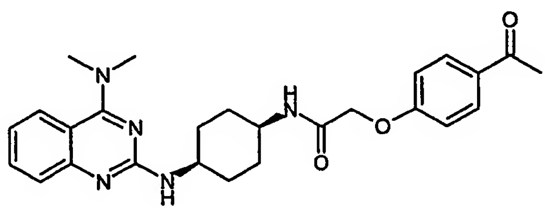
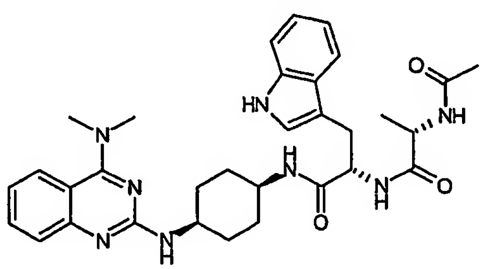
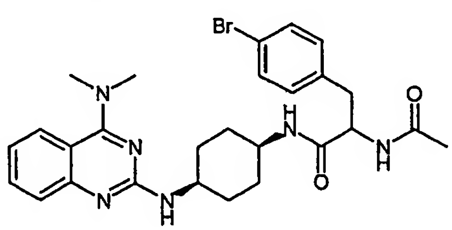
Example No.	Structure	APCI-MS
667		508 (M + H)
668		582 (M + H)
669		674 (M + H)
670		474 (M + H)
671		457 (M + H)

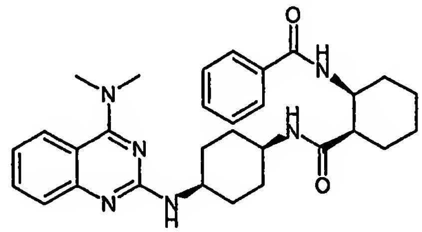
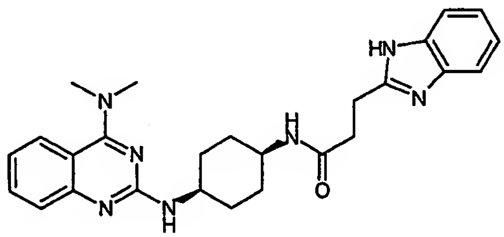
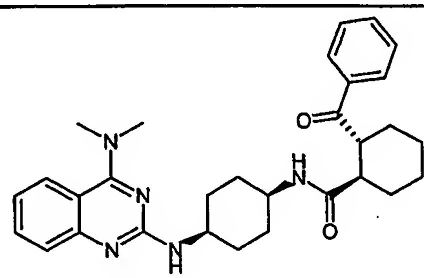
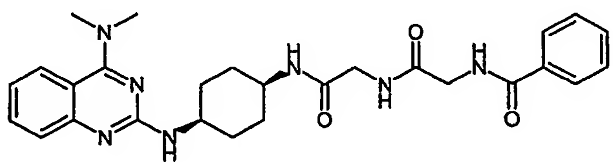
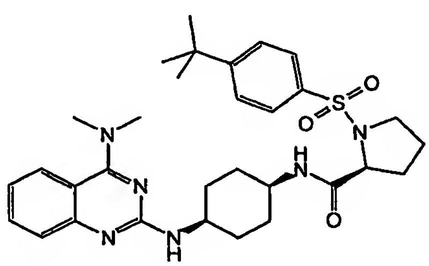
Example No.	Structure	APCI-MS
672		441 (M + H)
673		550 (M + H)
674		438 (M + H)
675		569 (M + H)
676		424 (M + H)

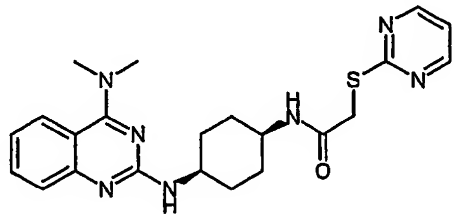
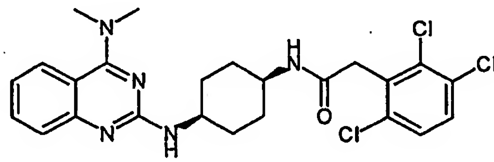
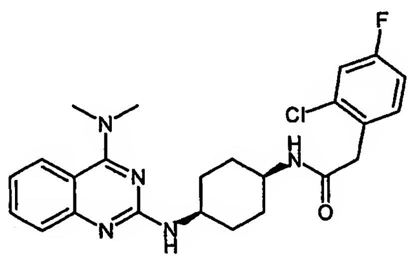
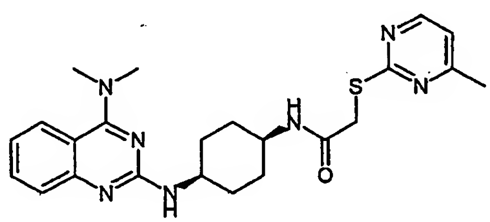
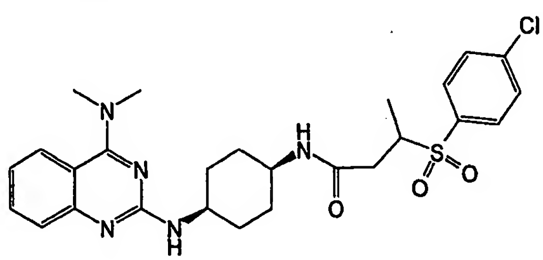
Example No.	Structure	APCI-MS
677		436 (M + H)
678		415 (M + H)
679		441 (M + H)
680		458 (M + H)
681		451 (M + H)

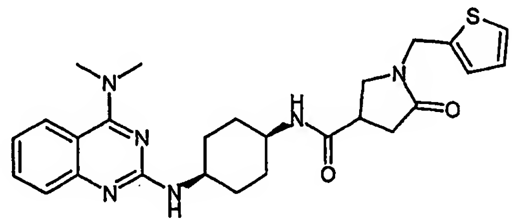
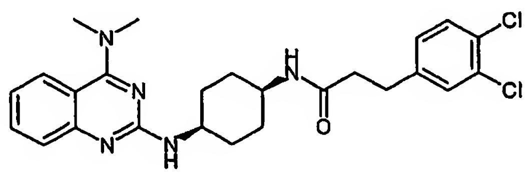
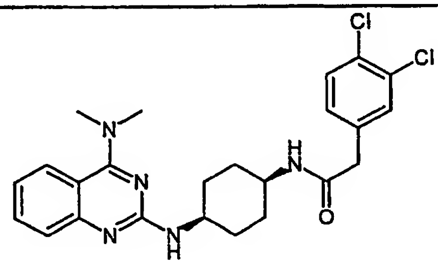
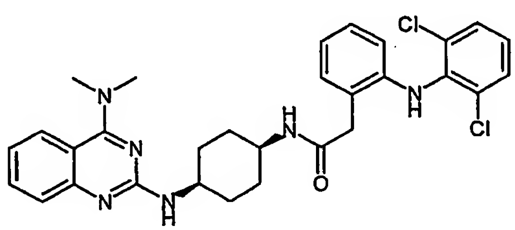
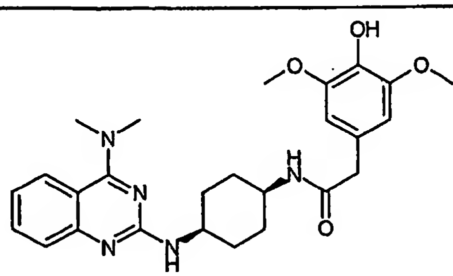
Example No.	Structure	APCI-MS
682		449 (M + H)
683		435 (M + H)
684		465 (M + H)
685		476 (M + H)
686		526 (M + H)

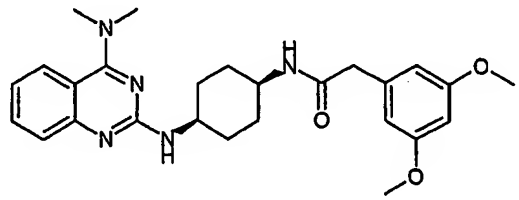
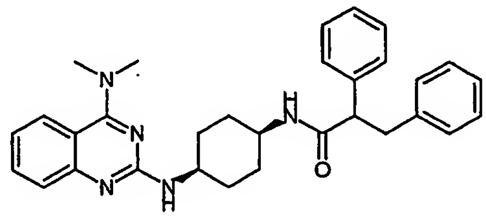
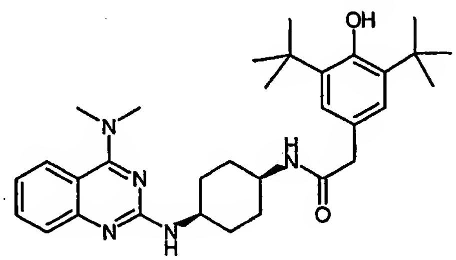
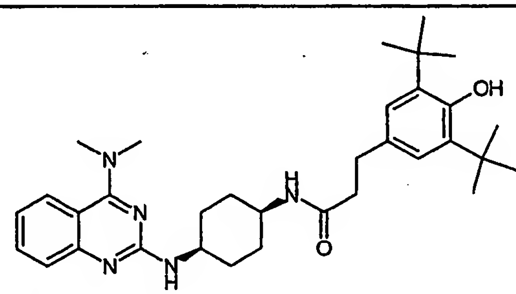
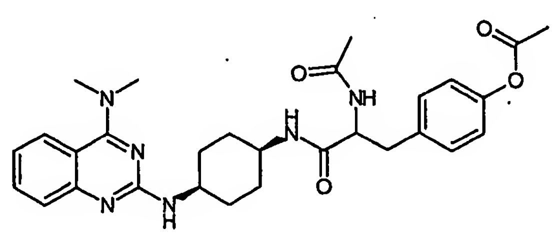
Example No.	Structure	APCI-MS
687		465 (M + H)
688		476 (M + H)
689		494 (M + H)
690		453 (M + H)
691		463 (M + H)

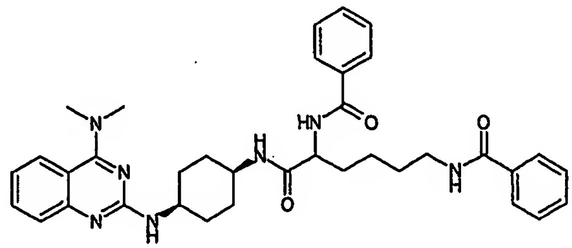
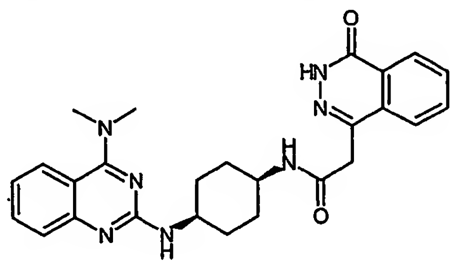
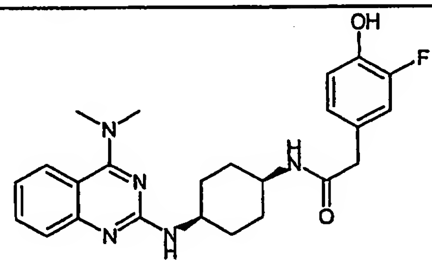
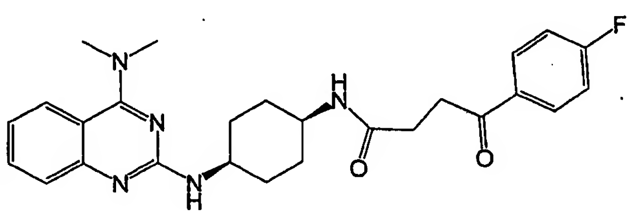
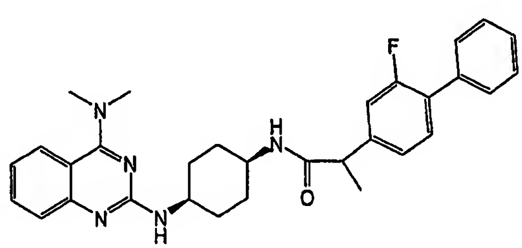
Example No.	Structure	APCI-MS
692		519 (M + H)
693		465 (M + H)
694		462 (M + H)
695		585 (M + H)
696		553 (M + H)

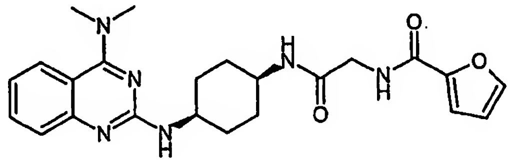
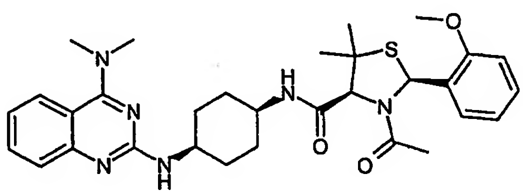
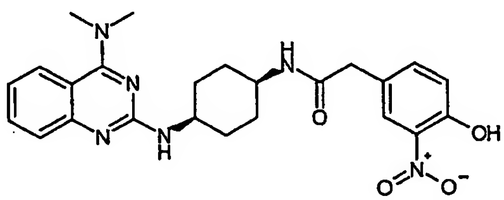
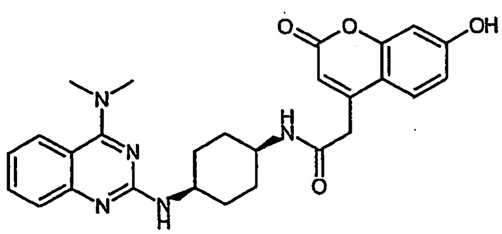
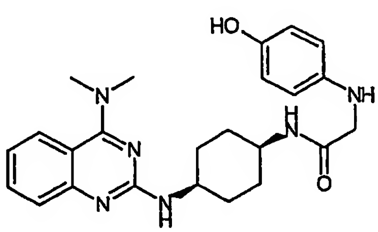
Example No.	Structure	APCI-MS
697		515 (M + H)
698		458 (M + H)
699		500 (M + H)
700		504 (M + H)
701		579 (M + H)

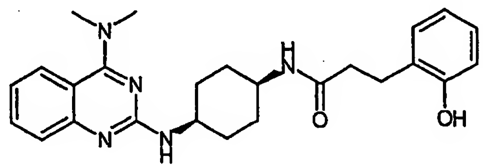
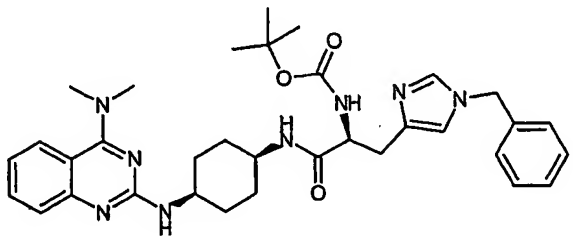
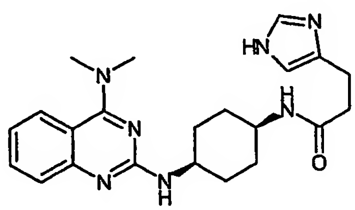
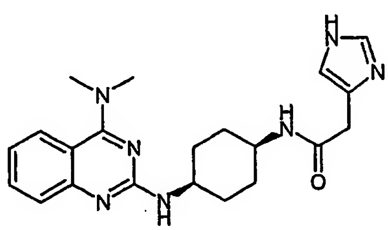
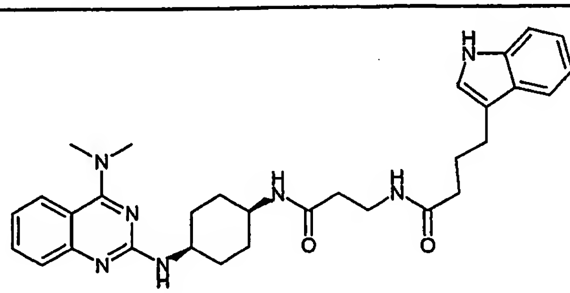
Example No.	Structure	APCI-MS
702		438 (M + H)
703		506 (M + H)
704		456 (M + H)
705		452 (M + H)
706		530 (M + H)

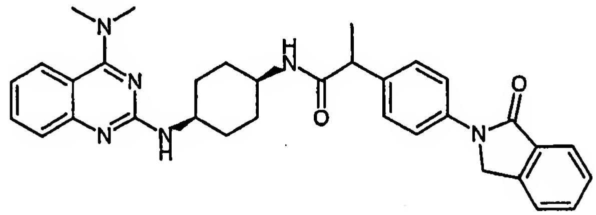
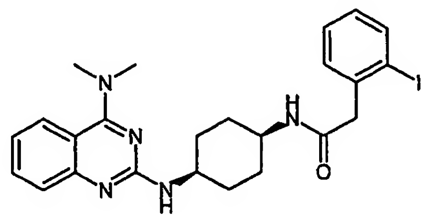
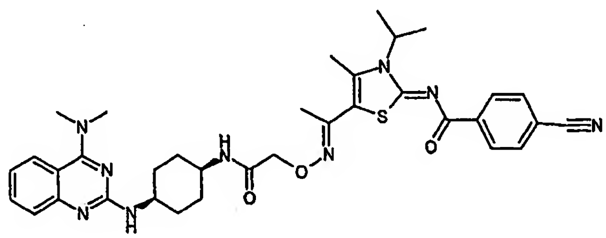
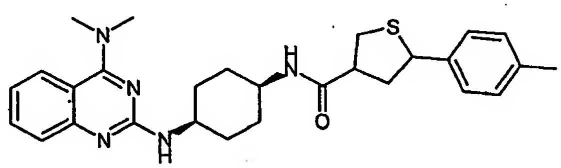
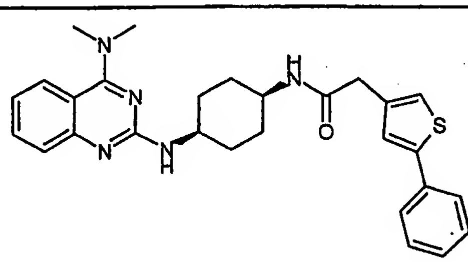
Example No.	Structure	APCI-MS
707		493 (M + H)
708		486 (M + H)
709		472 (M + H)
710		563 (M + H)
711		480 (M + H)

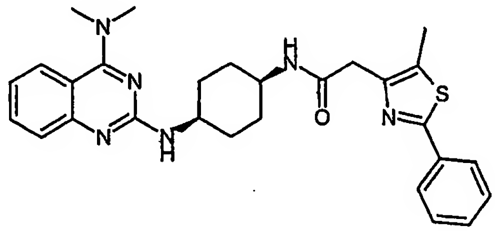
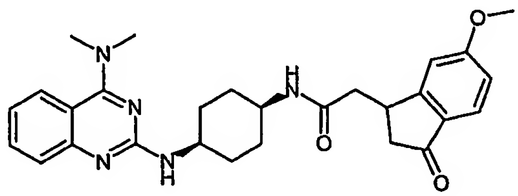
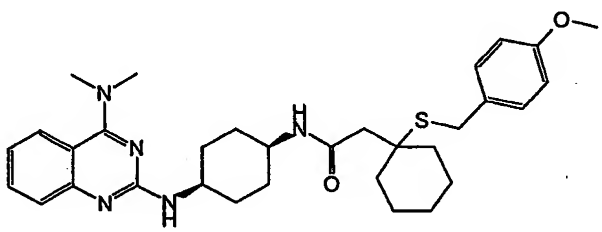
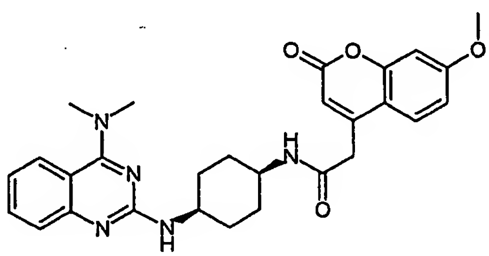
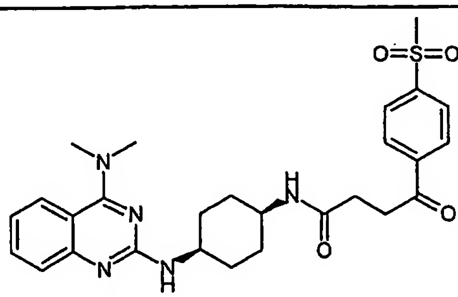
Example No.	Structure	APCI-MS
712		464 (M + H)
713		494 (M + H)
714		532 (M + H)
715		546 (M + H)
716		533 (M + H)

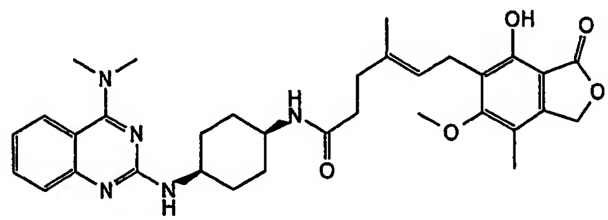
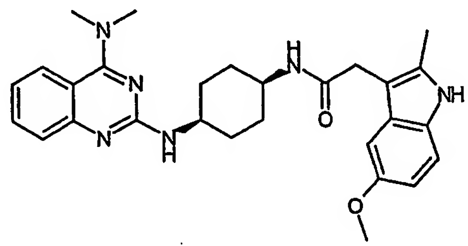
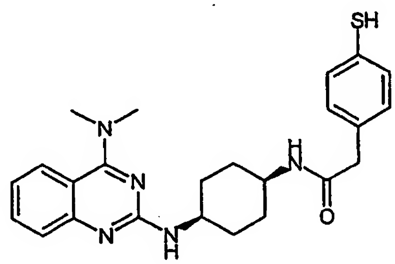
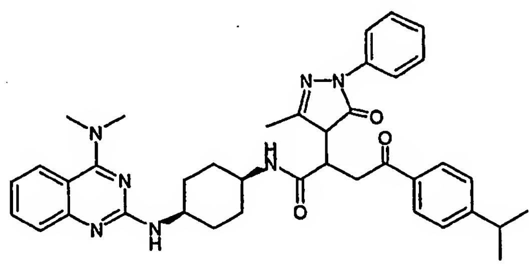
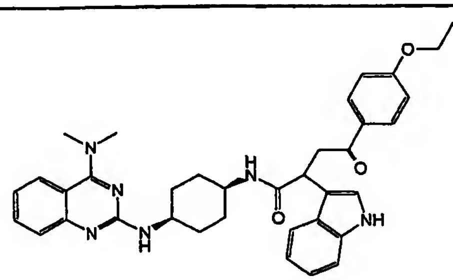
Example No.	Structure	APCI-MS
717		622 (M + H)
718		472 (M + H)
719		438 (M + H)
720		464 (M + H)
721		512 (M + H)

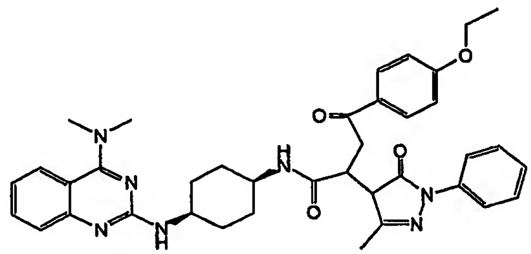
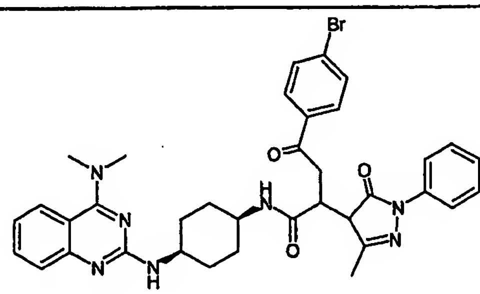
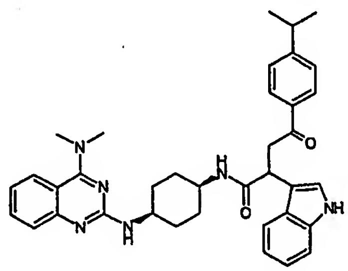
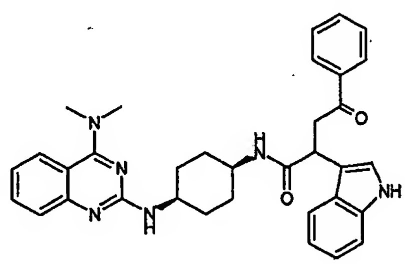
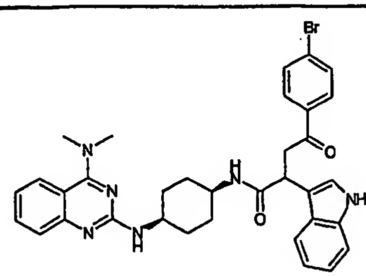
Example No.	Structure	APCI-MS
722		437 (M + H)
723		577 (M + H)
724		465 (M + H)
725		488 (M + H)
726		435 (M + H)

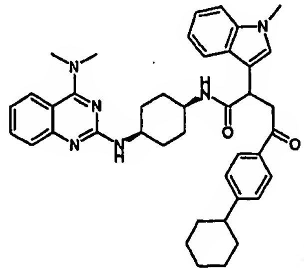
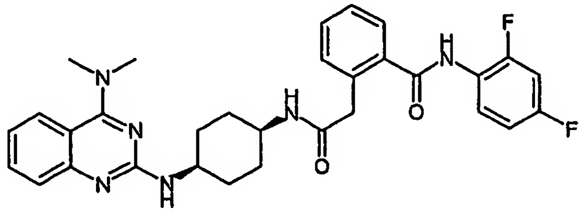
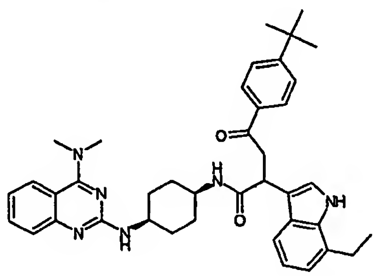
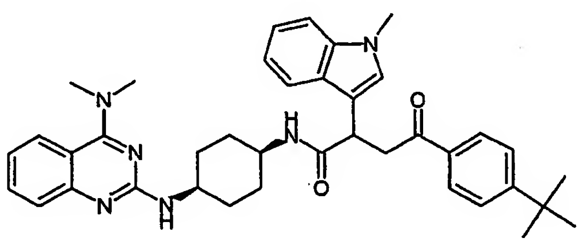
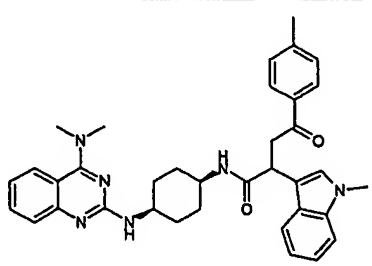
Example No.	Structure	APCI-MS
727		434 (M + H)
728		613 (M + H)
729		408 (M + H)
730		394 (M + H)
731		542 (M + H)

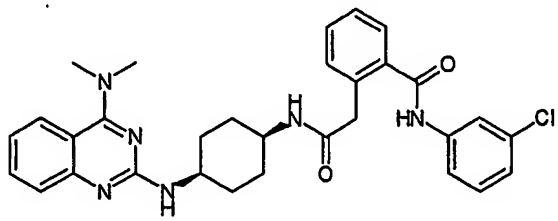
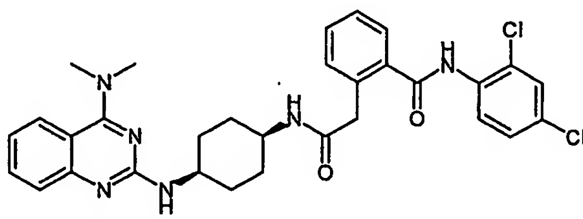
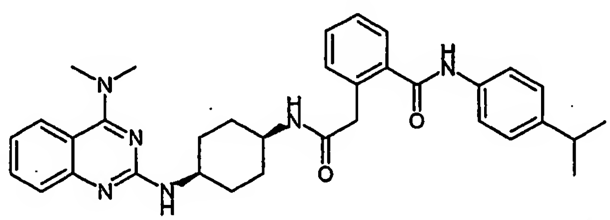
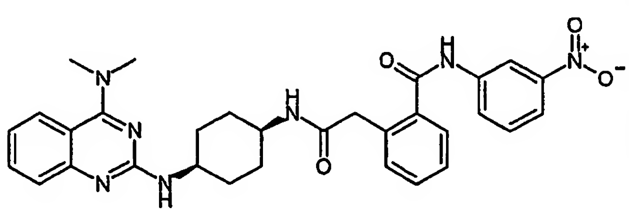
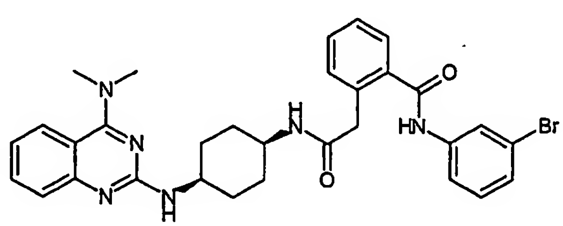
Example No.	Structure	APCI-MS
732		549 (M + H)
733		530 (M + H)
734		668 (M + H)
735		490 (M + H)
736		486 (M + H)

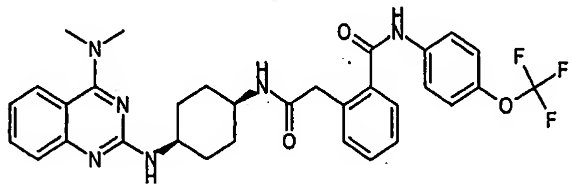
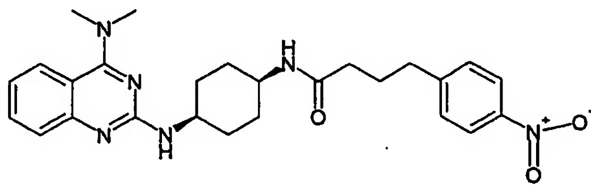
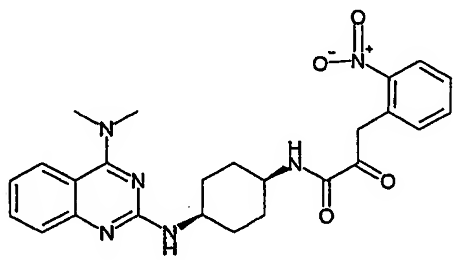
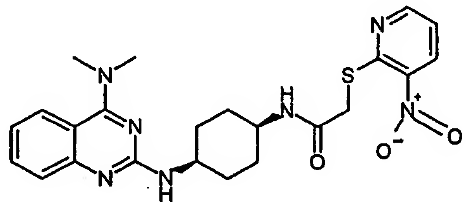
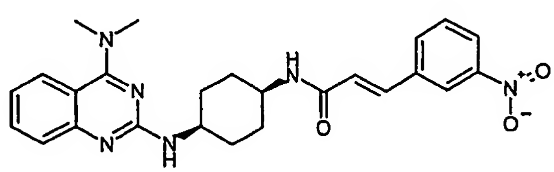
Example No.	Structure	APCI-MS
737		501 (M + H)
738		488 (M + H)
739		562 (M + H)
740		502 (M + H)
741		524 (M + H)

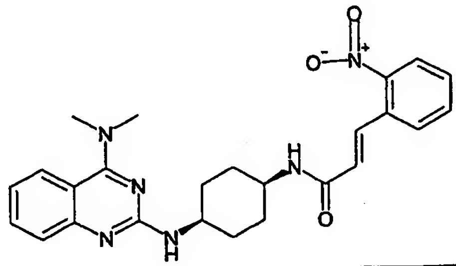
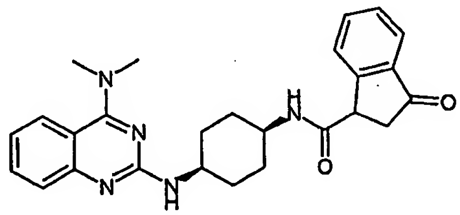
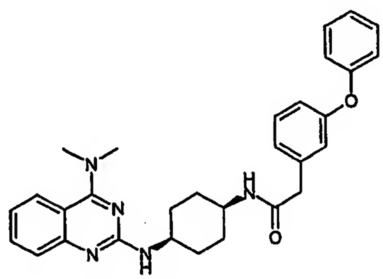
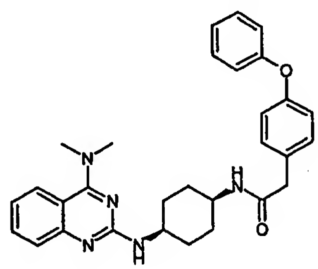
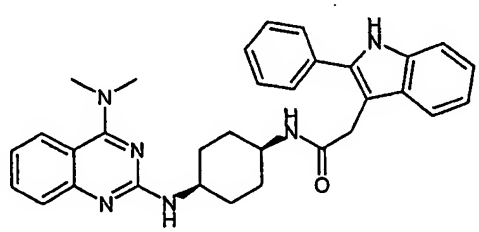
Example No.	Structure	APCI-MS
742		588 (M + H)
743		487 (M + H)
744		436 (M + H)
745		660 (M + H)
746		605 (M + H)

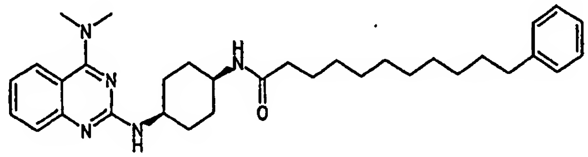
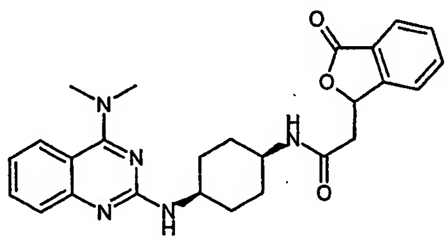
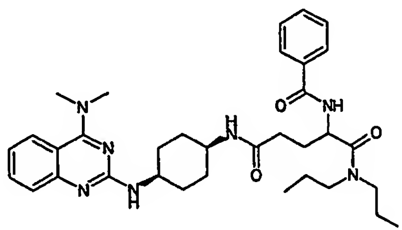
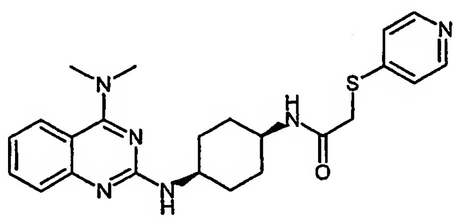
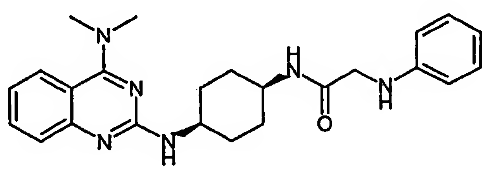
Example No.	Structure	APCI-MS
747		662 (M + H)
748		696 (M + H)
749		603 (M + H)
750		561 (M + H)
751		639 (M + H)

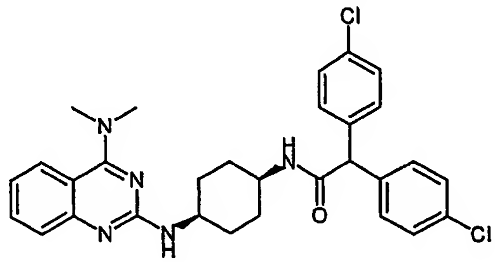
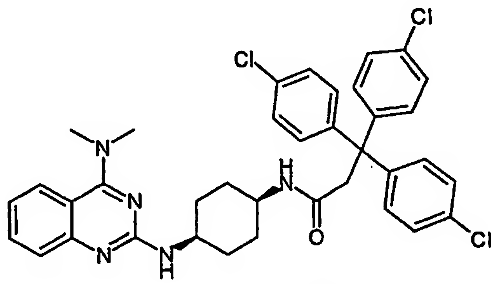
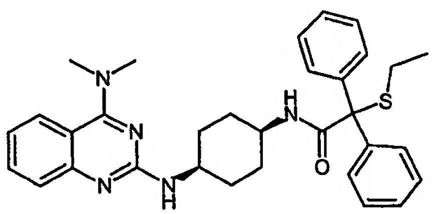
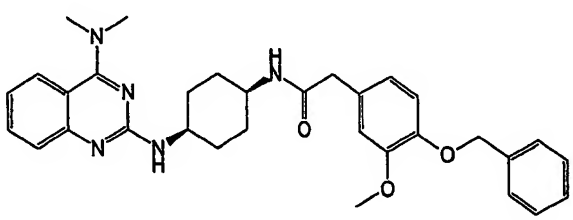
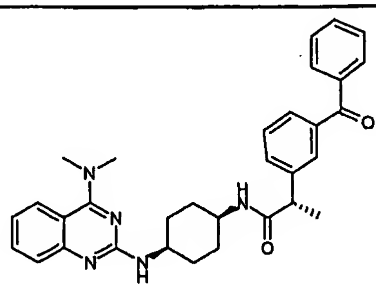
Example No.	Structure	APCI-MS
752		657 (M + H)
753		559 (M + H)
754		645 (M + H)
755		631 (M + H)
756		589 (M + H)

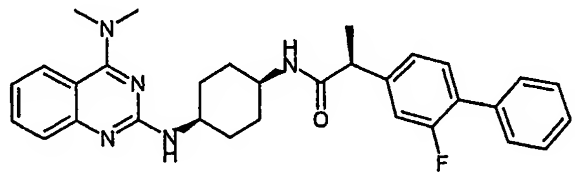
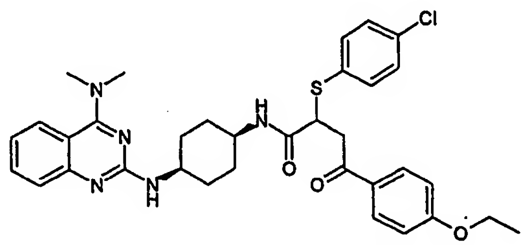
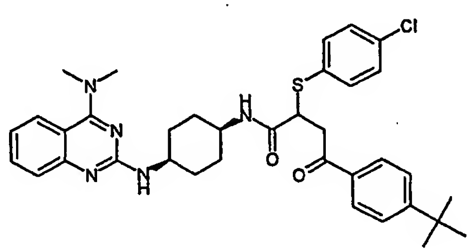
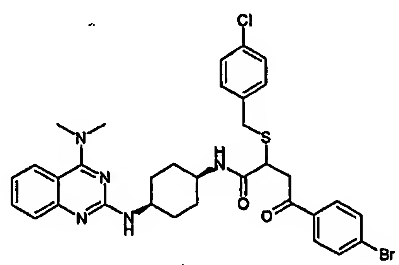
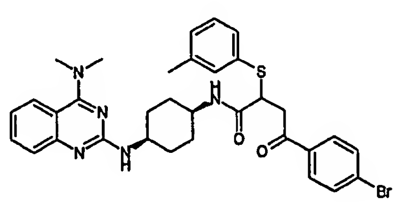
Example No.	Structure	APCI-MS
757		557 (M + H)
758		591 (M + H)
759		565 (M + H)
760		568 (M + H)
761		601 (M + H)

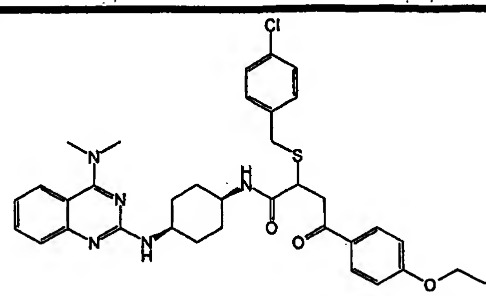
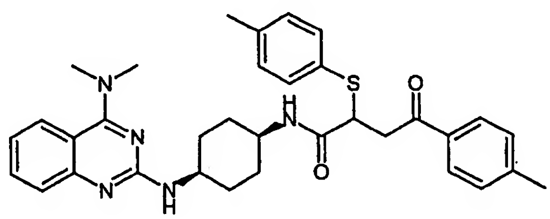
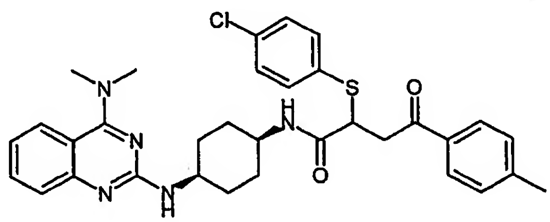
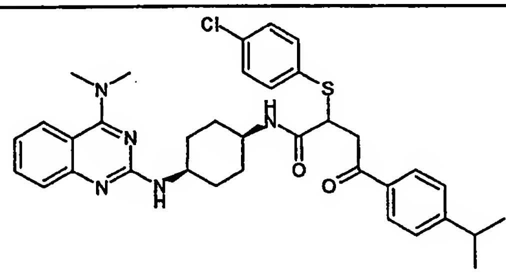
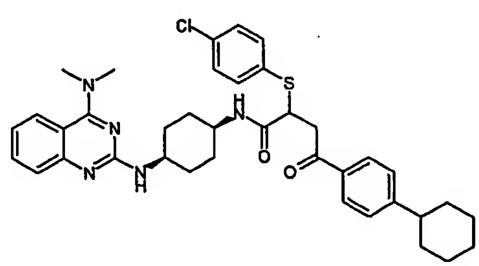
Example No.	Structure	APCI-MS
762		607 (M + H)
763		477 (M + H)
764		477 (M + H)
765		482 (M + H)
766		461 (M + H)

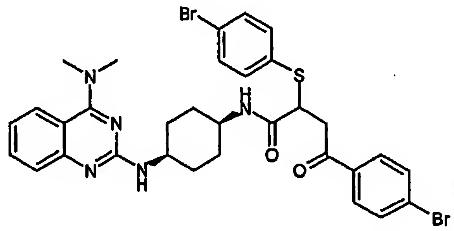
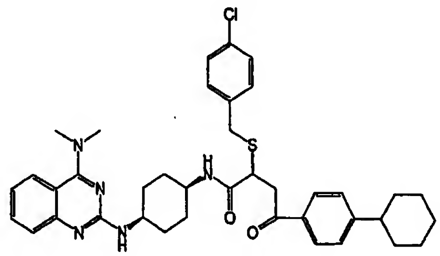
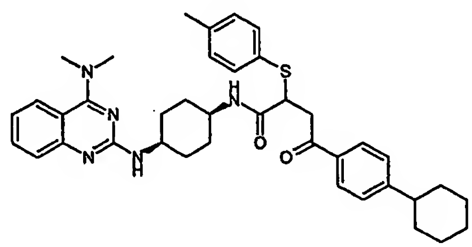
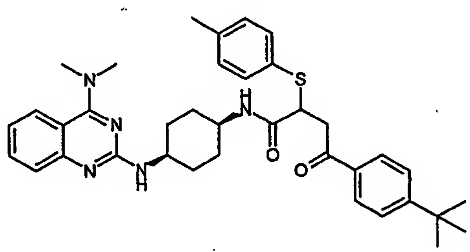
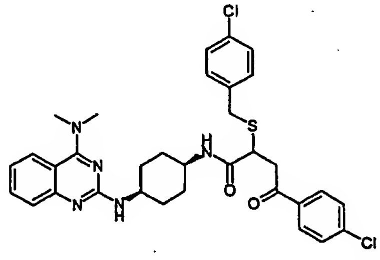
Example No.	Structure	APCI-MS
767		461 (M + H)
768		444 (M + H)
769		496 (M + H)
770		496 (M + H)
771		519 (M + H)

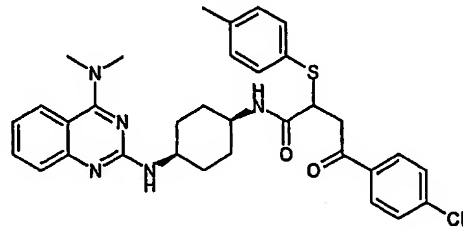
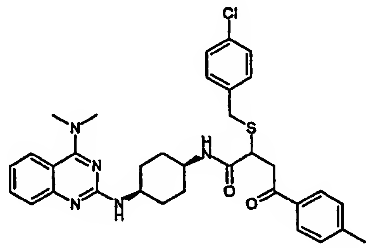
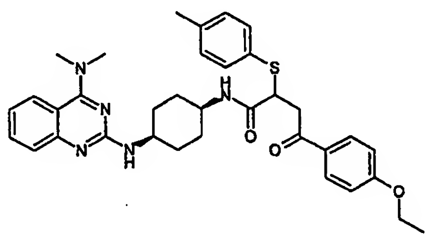
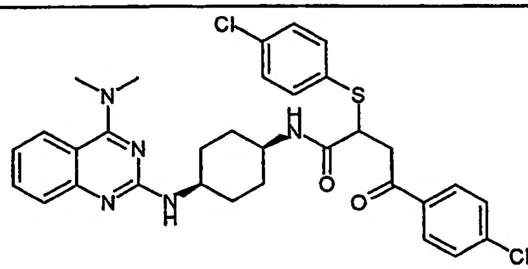
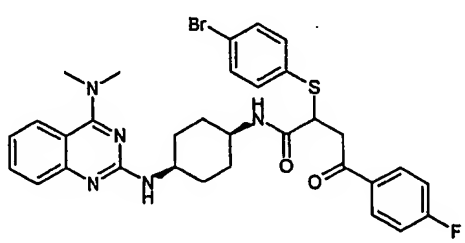
Example No.	Structure	APCI-MS
772		530 (M + H)
773		460 (M + H)
774		602 (M + H)
775		437 (M + H)
776		419 (M + H)

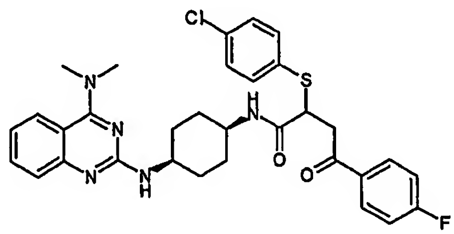
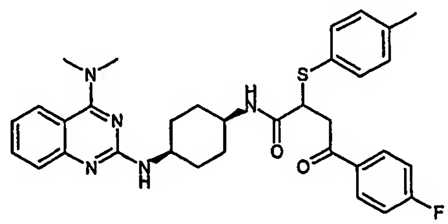
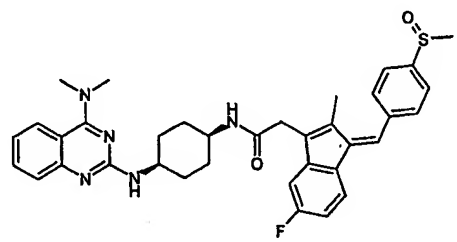
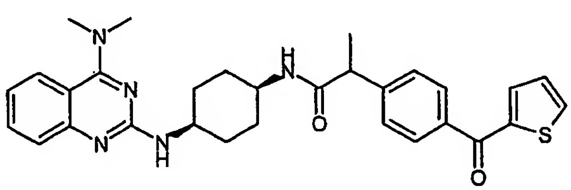
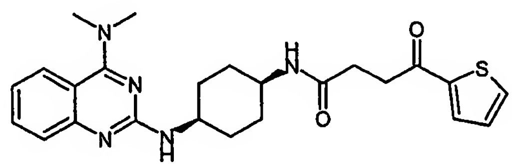
Example No.	Structure	APCI-MS
777		548 (M + H)
778		672 (M + H)
779		540 (M + H)
780		540 (M + H)
781		522 (M + H)

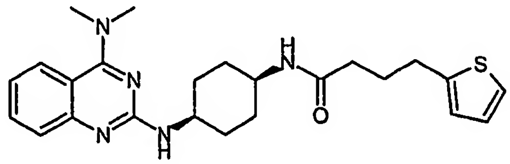
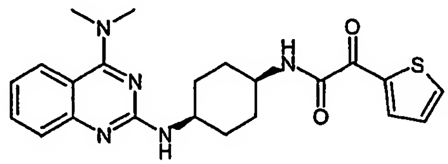
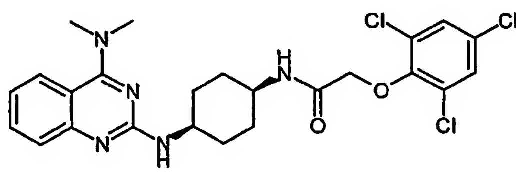
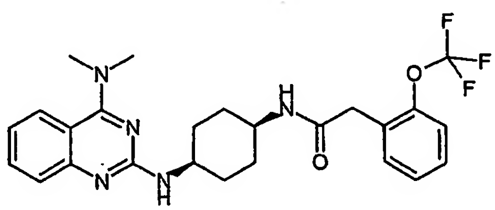
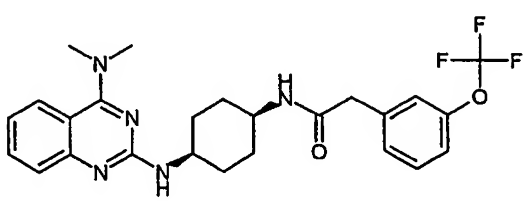
Example No.	Structure	APCI-MS
782		512 (M + H)
783		632 (M + H)
784		644 (M + H)
785		680 (M + H)
786		646 (M + H)

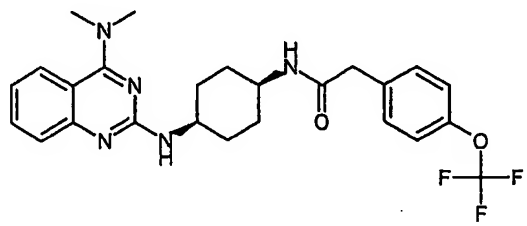
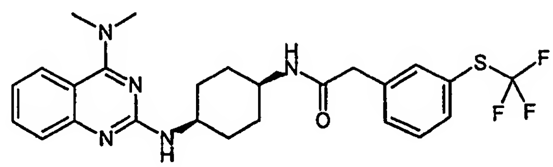
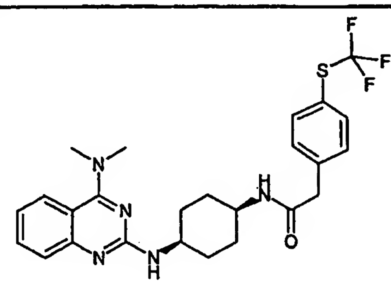
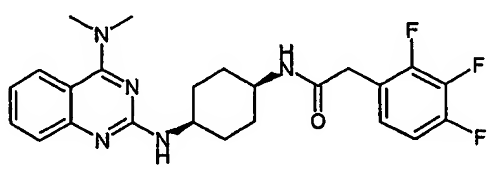
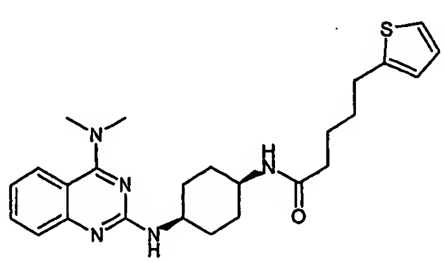
Example No.	Structure	APCI-MS
787		646 (M + H)
788		582 (M + H)
789		602 (M + H)
790		630 (M + H)
791		670 (M + H)

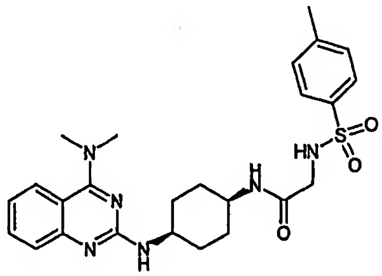
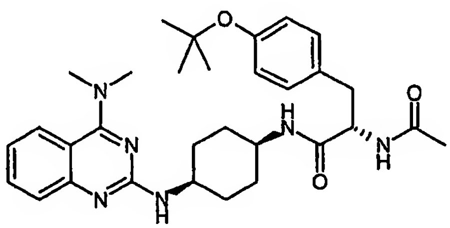
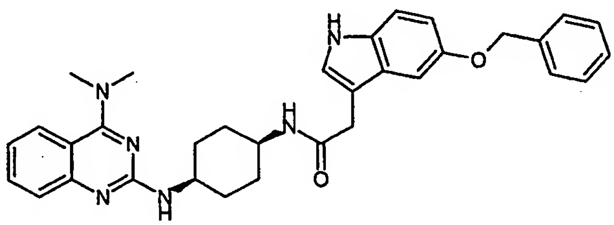
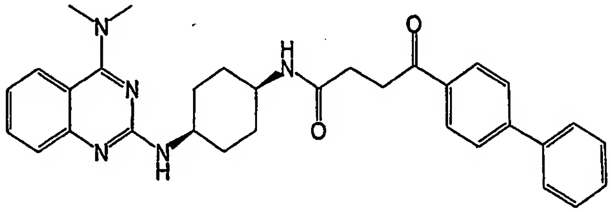
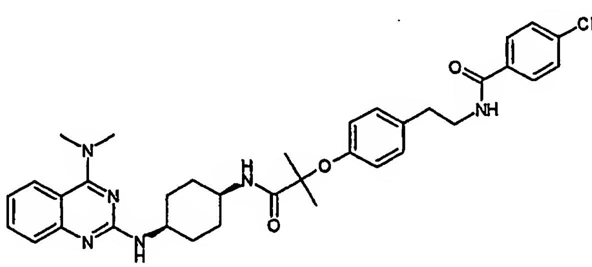
Example No.	Structure	APCI-MS
792		710 (M + H)
793		684 (M + H)
794		650 (M + H)
795		624 (M + H)
796		636 (M + H)

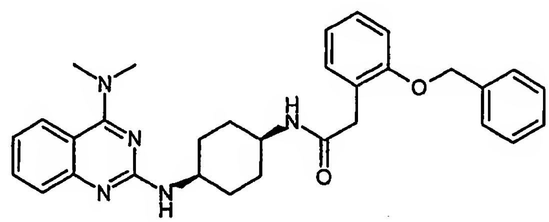
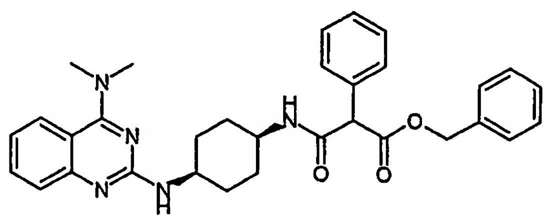
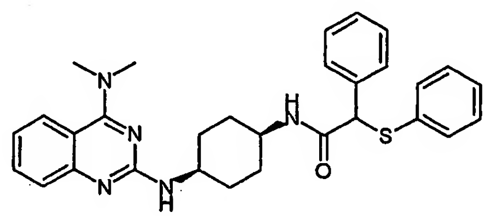
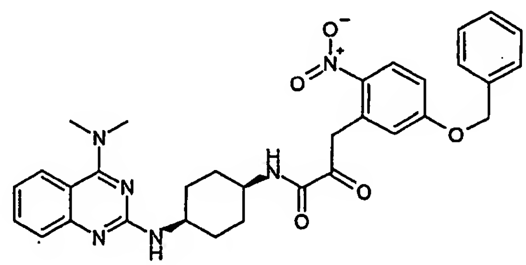
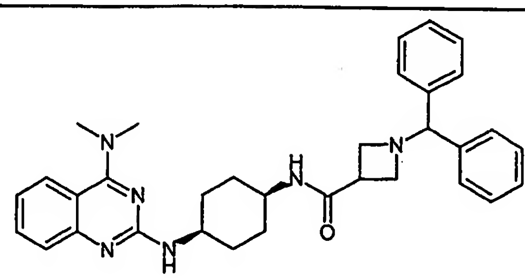
Example No.	Structure	APCI-MS
797		602 (M + H)
798		616 (M + H)
799		612 (M + H)
800		622 (M + H)
801		650 (M + H)

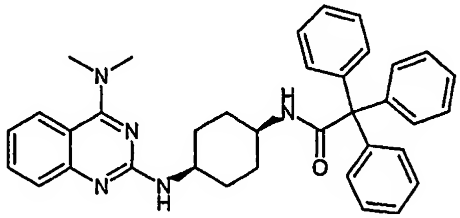
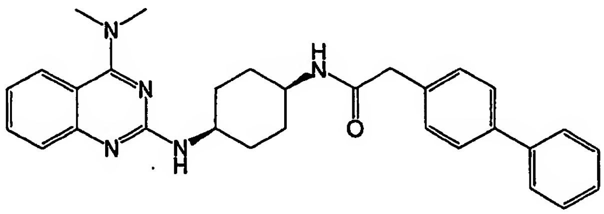
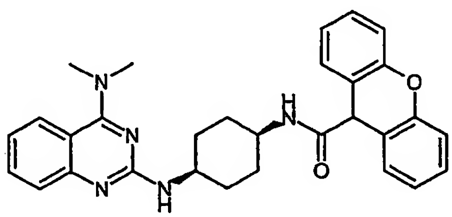
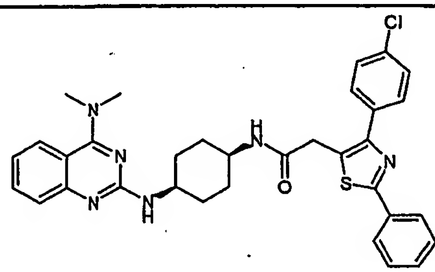
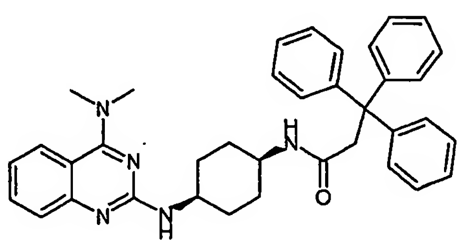
Example No.	Structure	APCI-MS
802		606 (M + H)
803		586 (M + H)
804		624 (M + H)
805		528 (M + H)
806		452 (M + H)

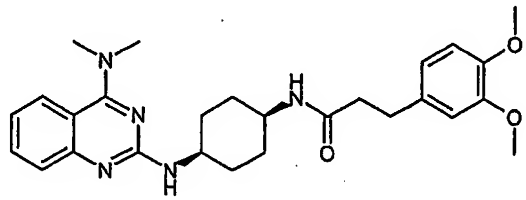
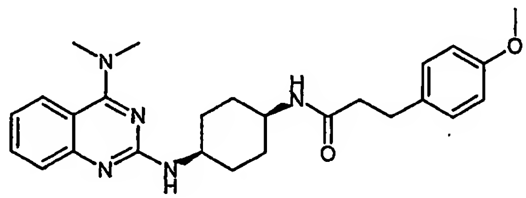
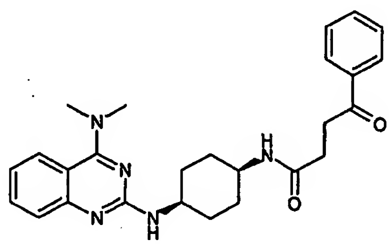
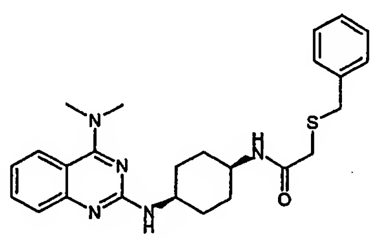
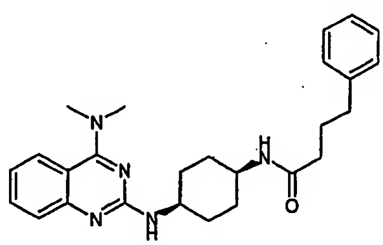
Example No.	Structure	APCI-MS
807		438 (M + H)
808		424 (M + H)
809		522 (M + H)
810		488 (M + H)
811		488 (M + H)

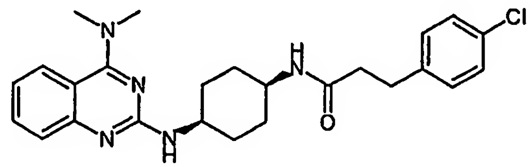
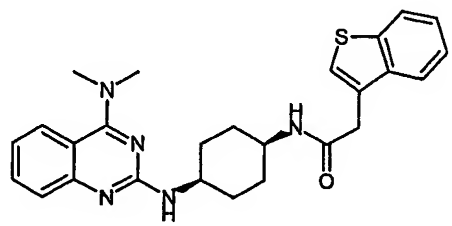
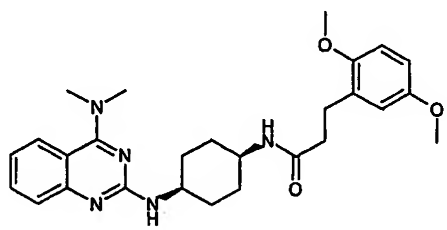
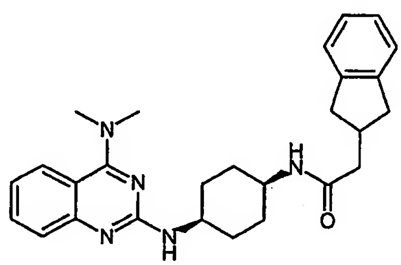
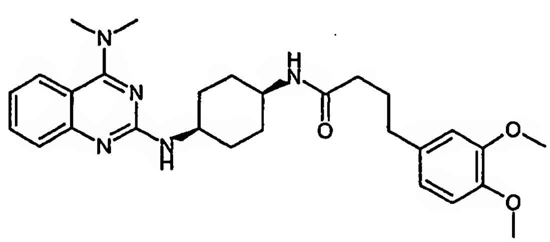
Example No.	Structure	APCI-MS
812		488 (M + H)
813		504 (M + H)
814		504 (M + H)
815		458 (M + H)
816		452 (M + H)

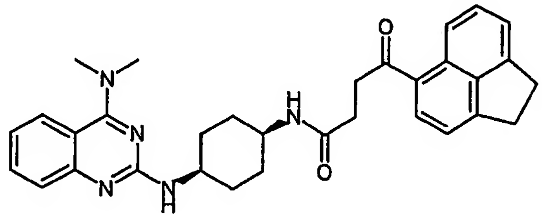
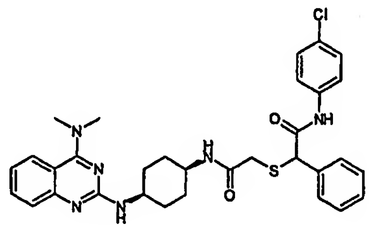
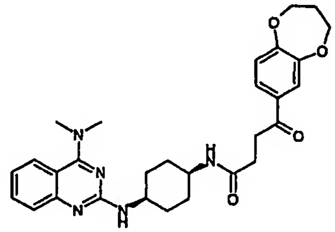
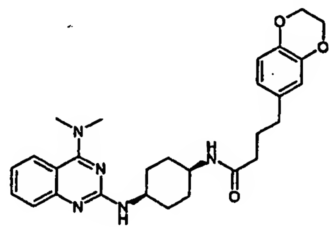
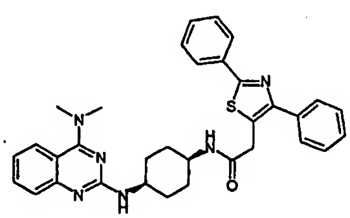
Example No.	Structure	APCI-MS
817		497 (M + H)
818		547 (M + H)
819		549 (M + H)
820		522 (M + H)
821		629 (M + H)

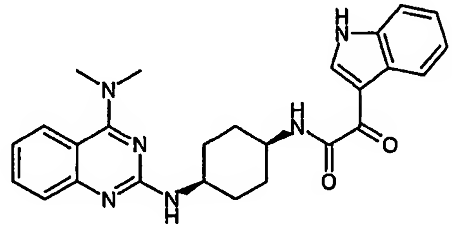
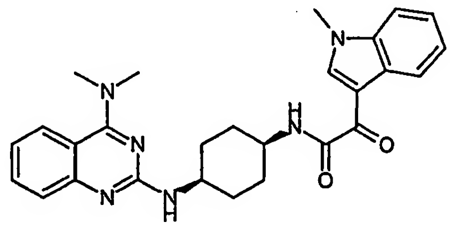
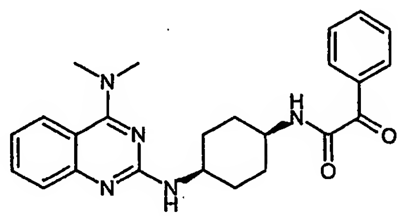
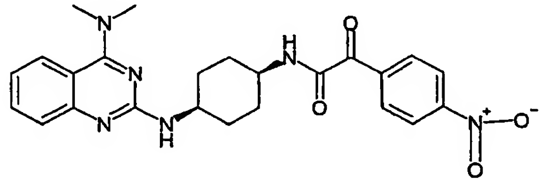
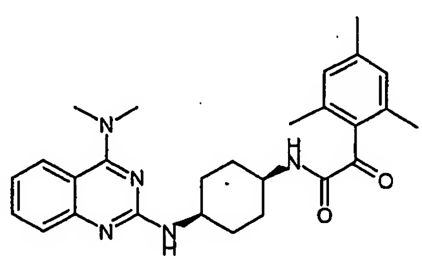
Example No.	Structure	APCI-MS
822		510 (M + H)
823		538 (M + H)
824		512 (M + H)
825		583 (M + H)
826		535 (M + H)

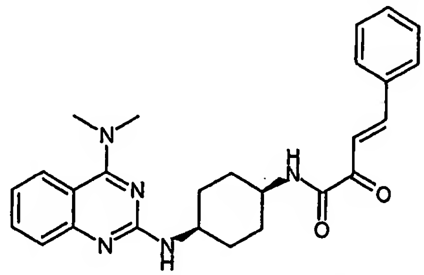
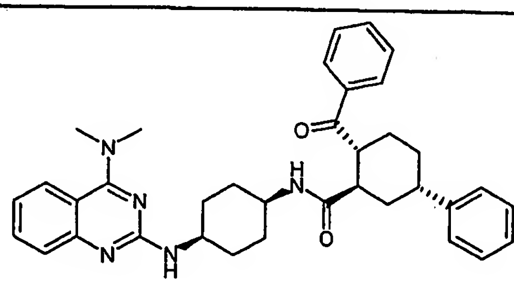
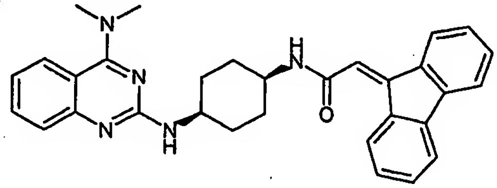
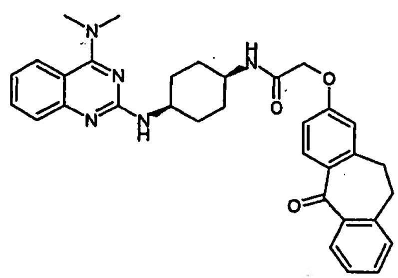
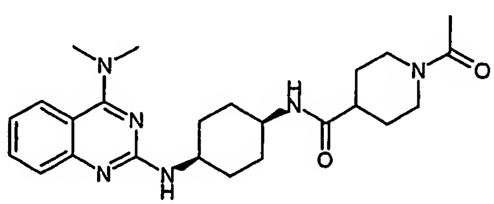
Example No.	Structure	APCI-MS
827		556 (M + H)
828		480 (M + H)
829		494 (M + H)
830		597 (M + H)
831		570 (M + H)

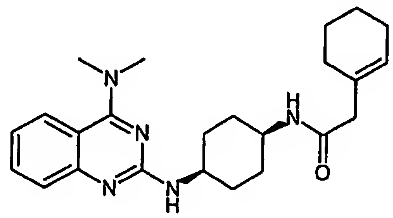
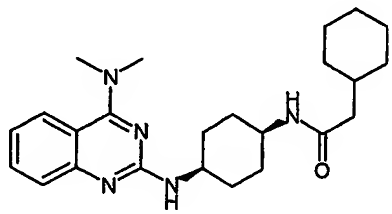
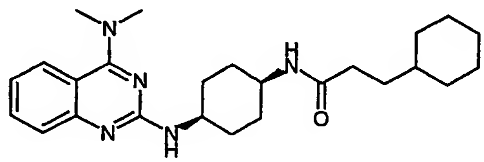
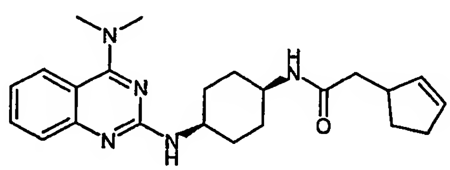
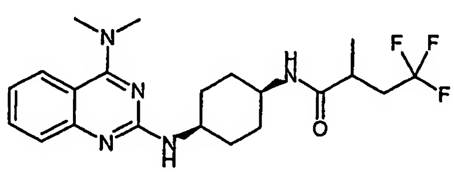
Example No.	Structure	APCI-MS
832		478 (M + H)
833		448 (M + H)
834		446 (M + H)
835		450 (M + H)
836		432 (M + H)

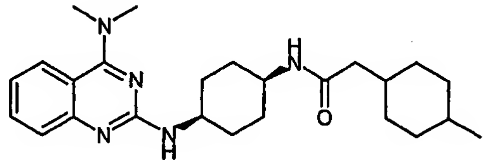
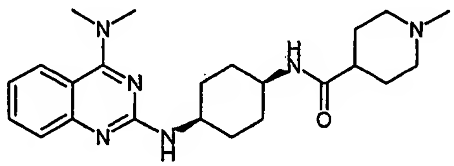
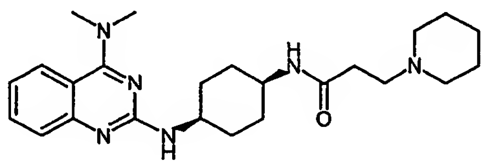
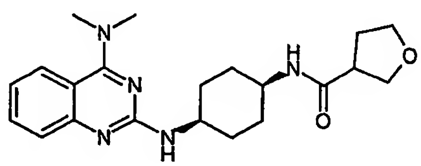
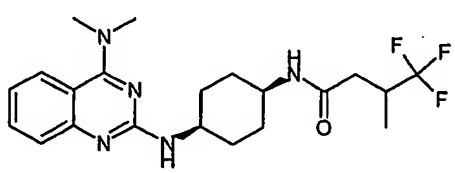
Example No.	Structure	APCI-MS
837		452 (M + H)
838		460 (M + H)
839		478 (M + H)
840		444 (M + H)
841		492 (M + H)

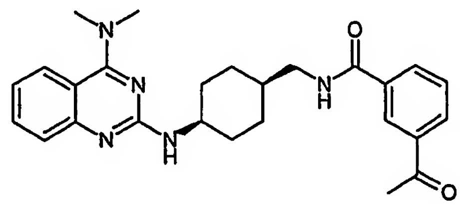
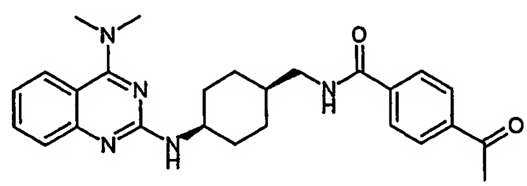
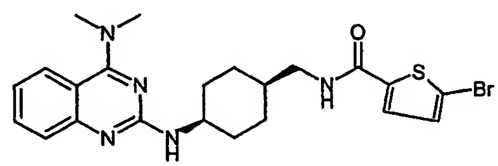
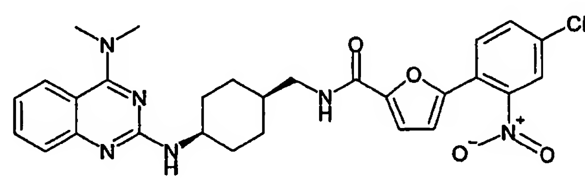
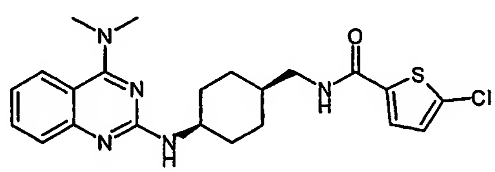
Example No.	Structure	APCI-MS
842		522 (M + H)
843		603 (M + H)
844		518 (M + H)
845		490 (M + H)
846		563 (M + H)

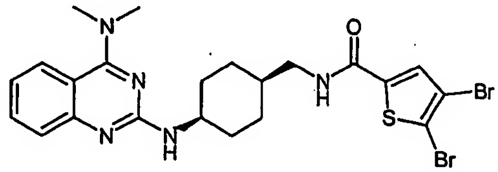
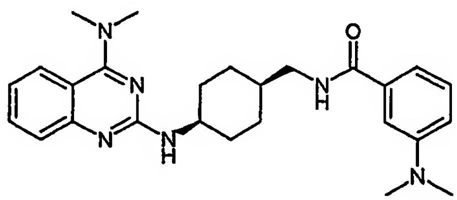
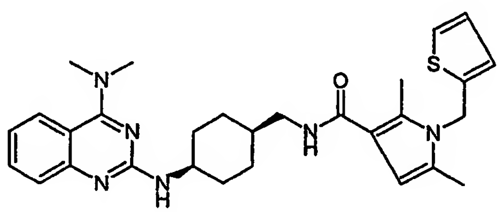
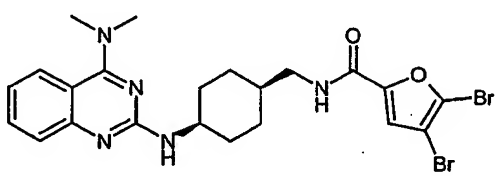
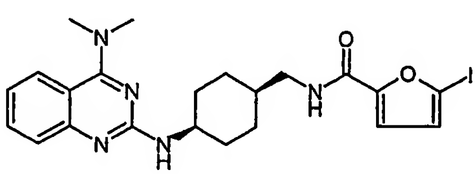
Example No.	Structure	APCI-MS
847		457 (M + H)
848		471 (M + H)
849		418 (M + H)
850		463 (M + H)
851		460 (M + H)

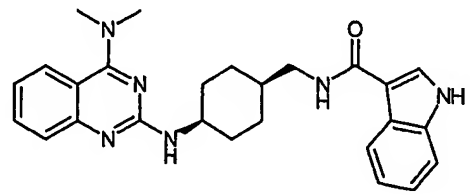
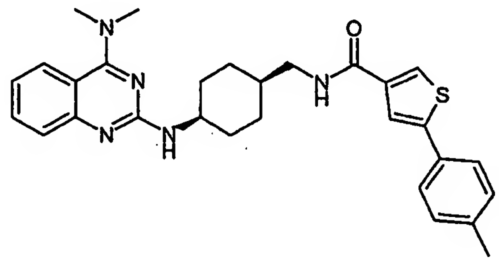
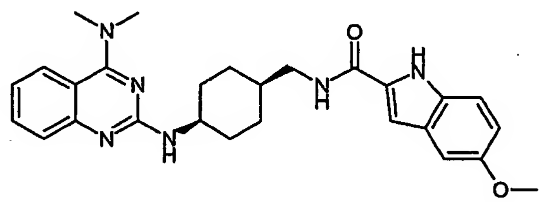
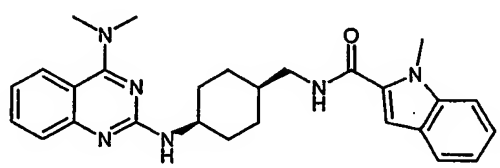
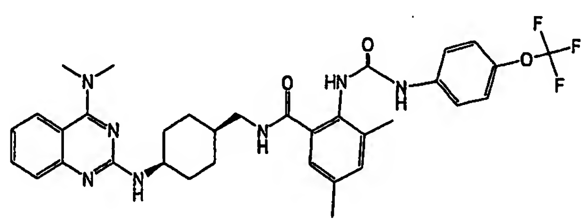
Example No.	Structure	APCI-MS
852		444 (M + H)
853		576 (M + H)
854		490 (M + H)
855		550 (M + H)
856		439 (M + H)

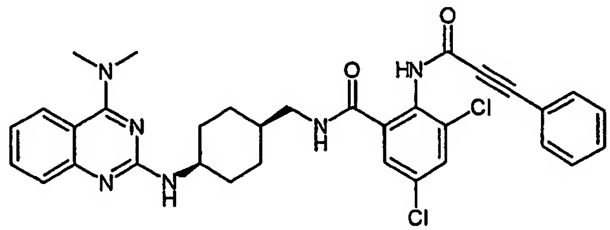
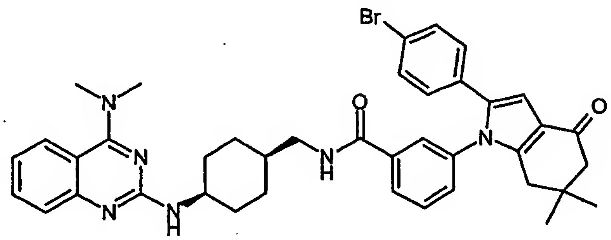
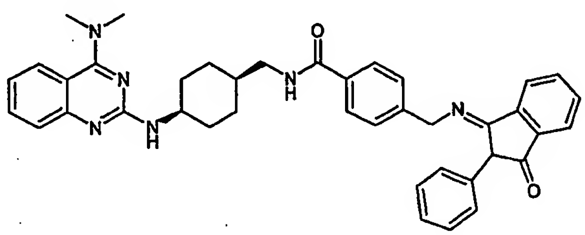
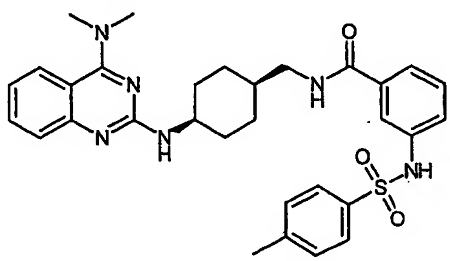
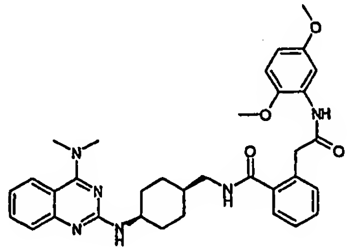
Example No.	Structure	APCI-MS
857		408 (M + H)
858		410 (M + H)
859		424 (M + H)
860		394 (M + H)
861		424 (M + H)

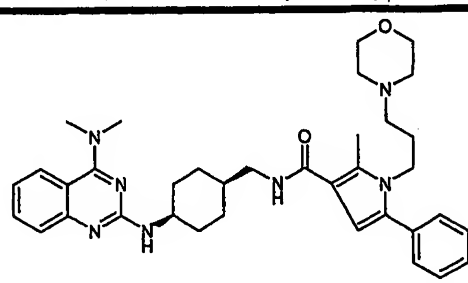
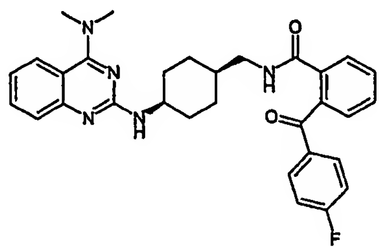
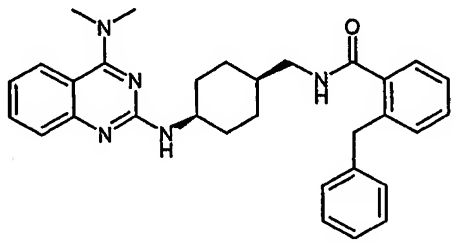
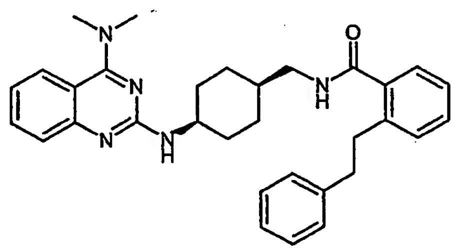
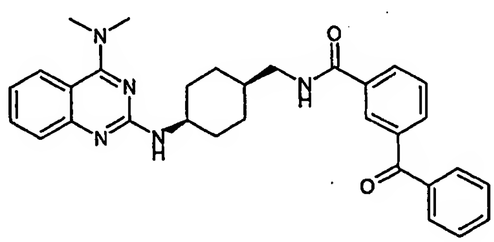
Example No.	Structure	APCI-MS
862		424 (M + H)
863		411 (M + H)
864		425 (M + H)
865		384 (M + H)
866		424 (M + H)

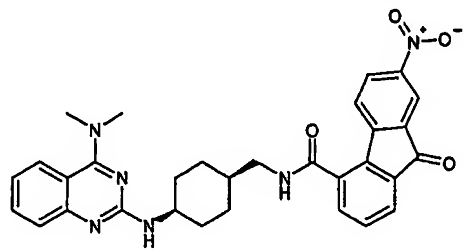
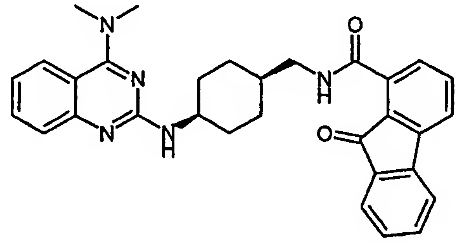
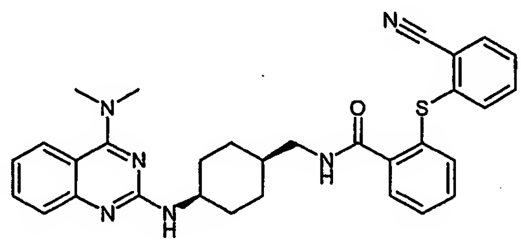
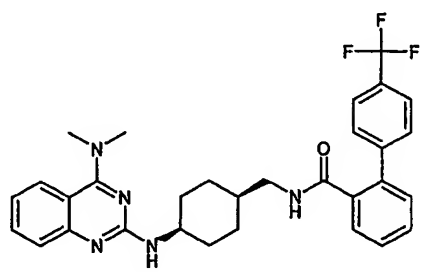
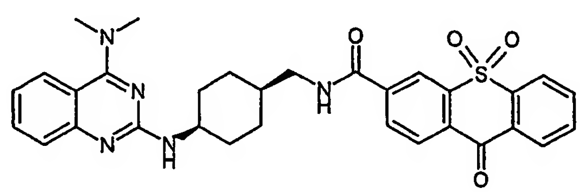
Example No.	Structure	APCI-MS
867		446 (M + H)
868		446 (M + H)
869		488 (M + H)
870		549 (M + H)
871		444 (M + H)

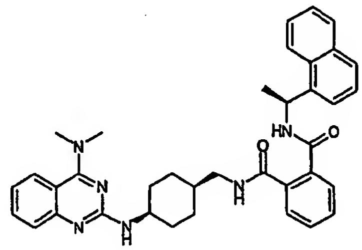
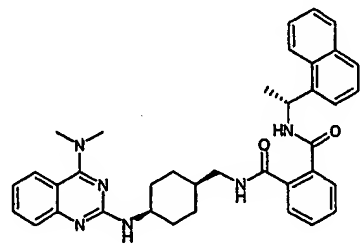
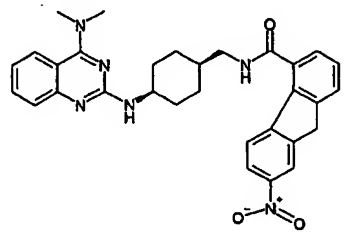
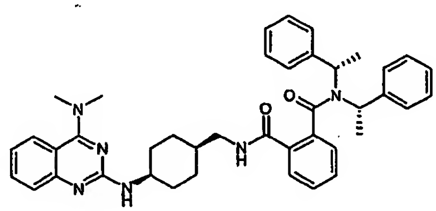
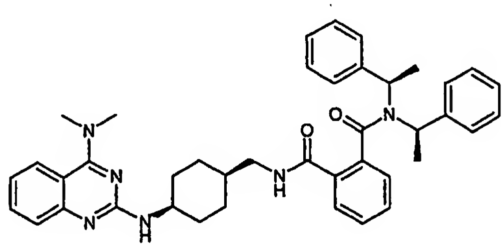
Example No.	Structure	APCI-MS
872		566 (M + H)
873		447 (M + H)
874		517 (M + H)
875		550 (M + H)
876		520 (M + H)

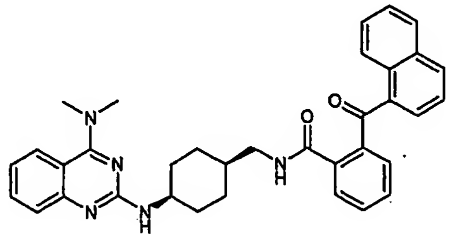
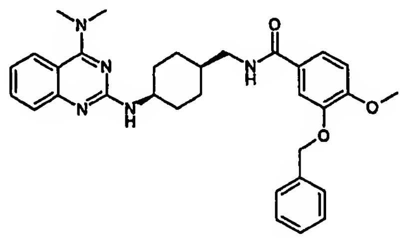
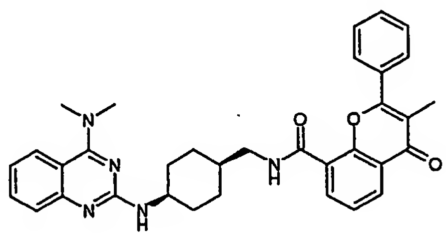
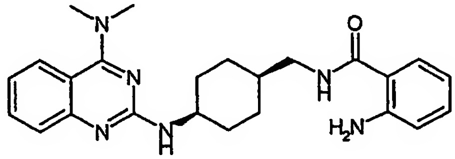
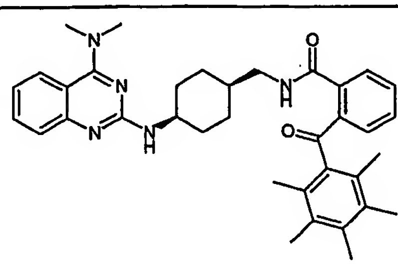
Example No.	Structure	APCI-MS
877		443 (M + H)
878		500 (M + H)
879		473 (M + H)
880		457 (M + H)
881		650 (M + H)

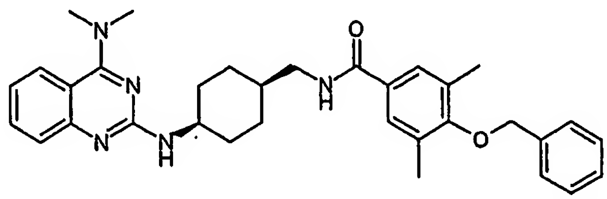
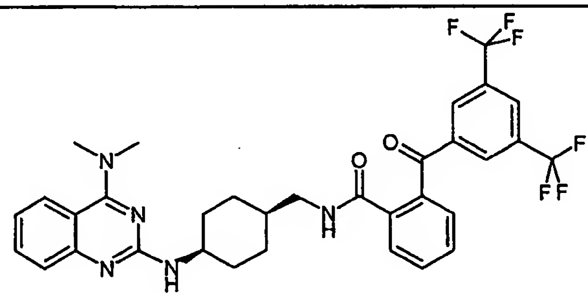
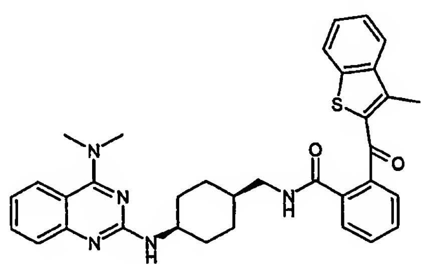
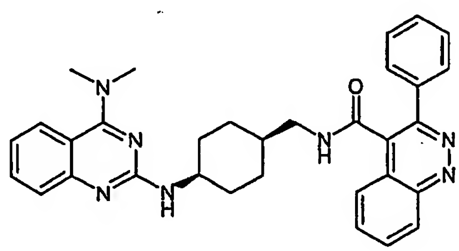
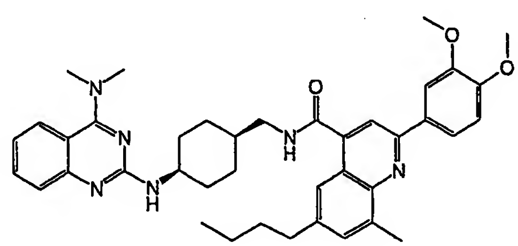
Example No.	Structure	APCI-MS
882		615 (M + H)
883		719 (M + H)
884		637 (M + H)
885		573 (M + H)
886		597 (M + H)

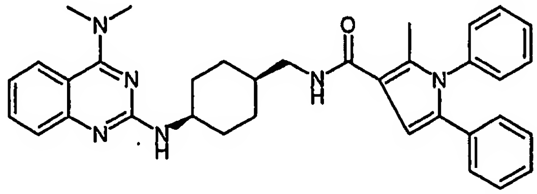
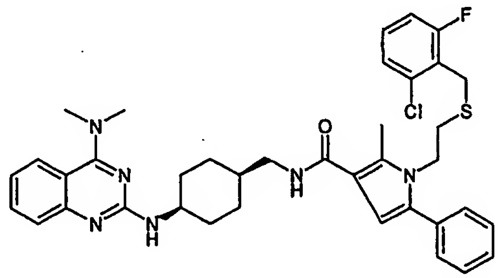
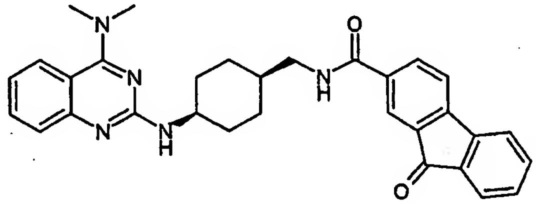
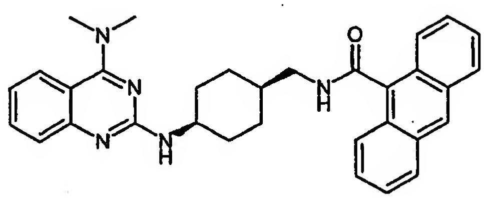
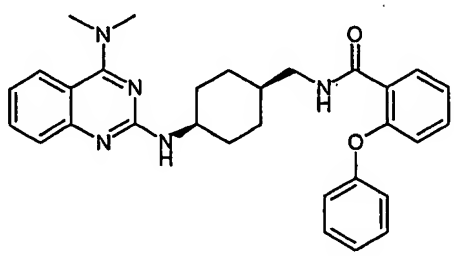
Example No.	Structure	APCI-MS
887		610 (M + H)
888		526 (M + H)
889		494 (M + H)
890		508 (M + H)
891		508 (M + H)

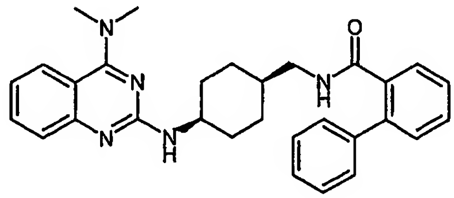
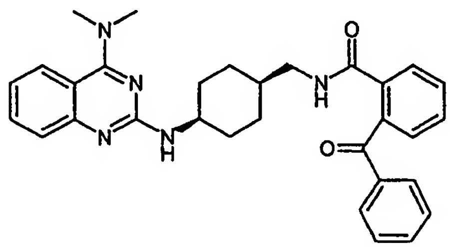
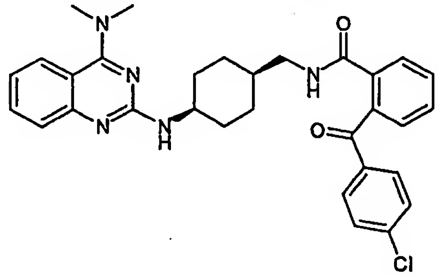
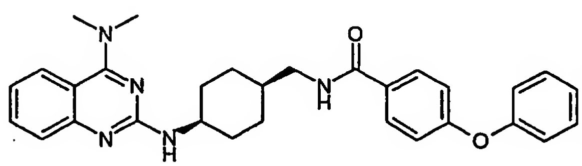
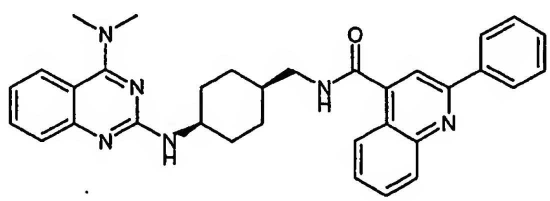
Example No.	Structure	APCI-MS
892		551 (M + H)
893		506 (M + H)
894		537 (M + H)
895		548 (M + H)
896		570 (M + H)

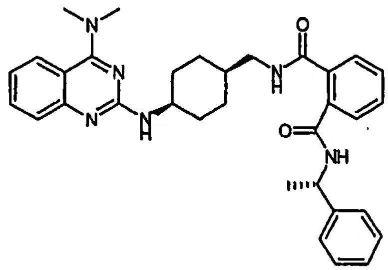
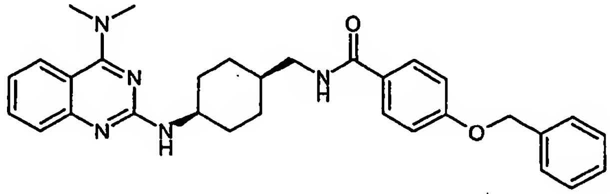
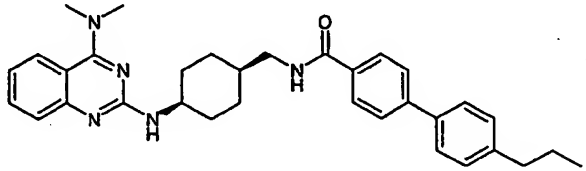
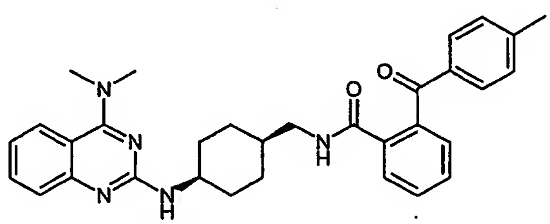
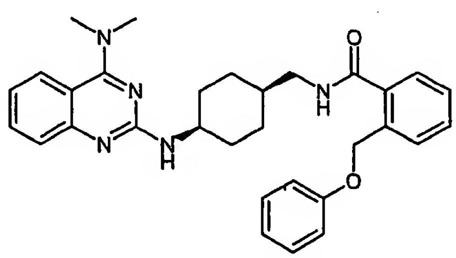
Example No.	Structure	APCI-MS
897		601 (M + H)
898		601 (M + H)
899		537 (M + H)
900		655 (M + H)
901		655 (M + H)

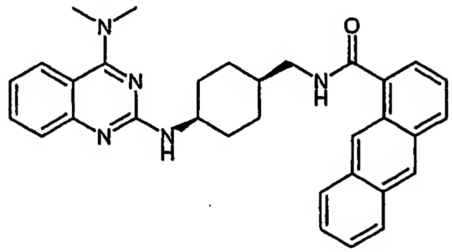
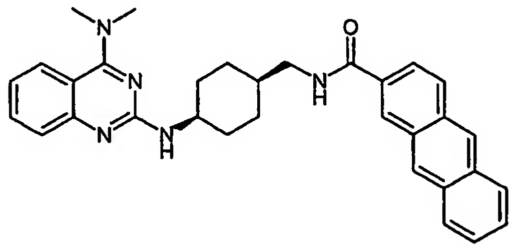
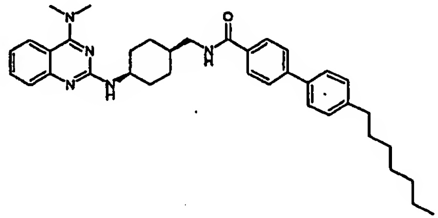
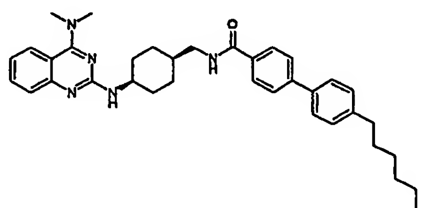
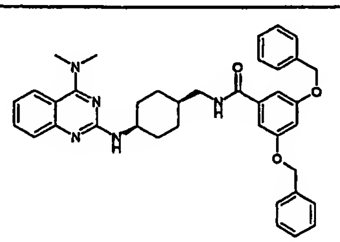
Example No.	Structure	APCI-MS
902		558 (M + H)
903		540 (M + H)
904		562 (M + H)
905		419 (M + H)
906		578 (M + H)

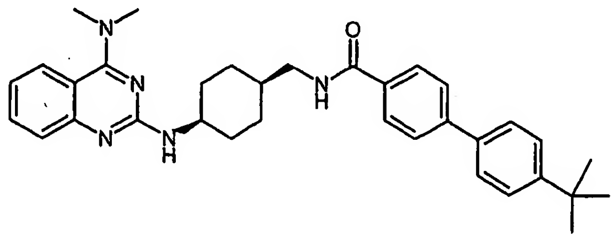
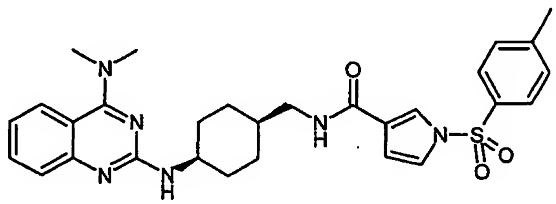
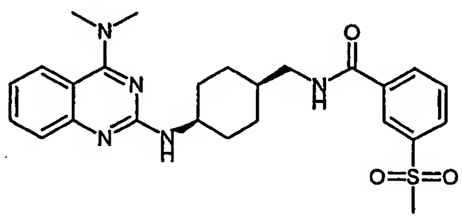
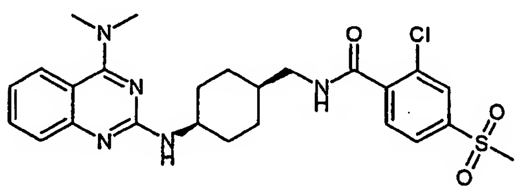
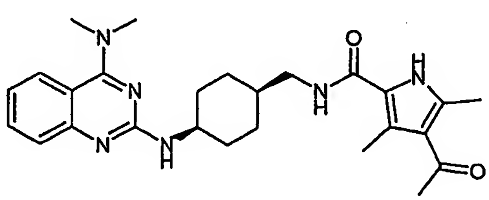
Example No.	Structure	APCI-MS
907		538 (M + H)
908		644 (M + H)
909		578 (M + H)
910		532 (M + H)
911		661 (M + H)

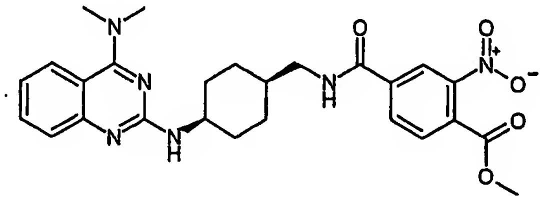
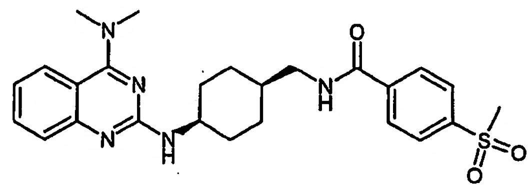
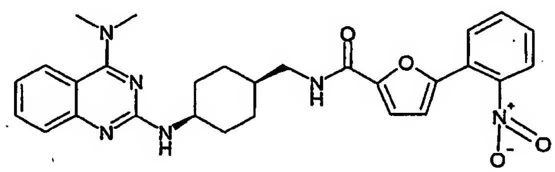
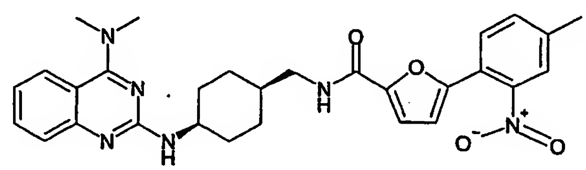
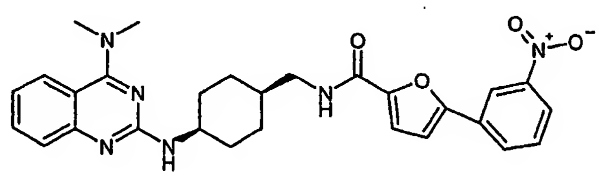
Example No.	Structure	APCI-MS
912		559 (M + H)
913		685 (M + H)
914		506 (M + H)
915		504 (M + H)
916		496 (M + H)

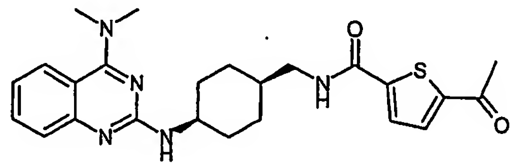
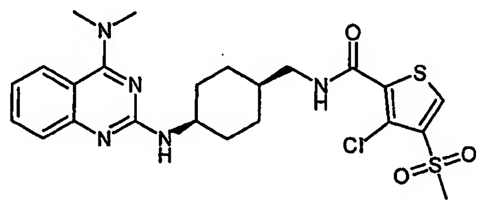
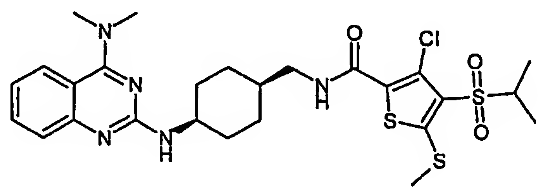
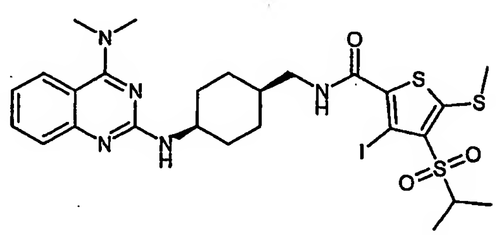
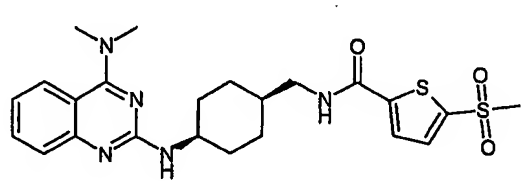
Example No.	Structure	APCI-MS
917		480 (M + H)
918		508 (M + H)
919		542 (M + H)
920		496 (M + H)
921		531 (M + H)

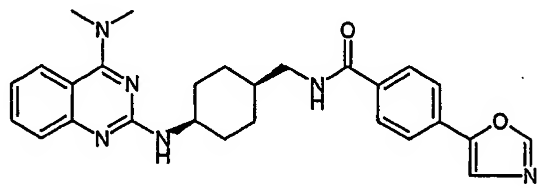
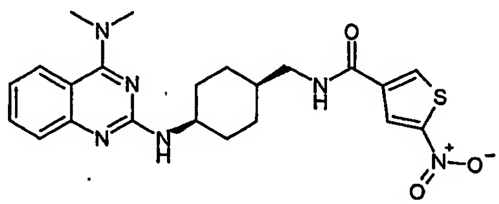
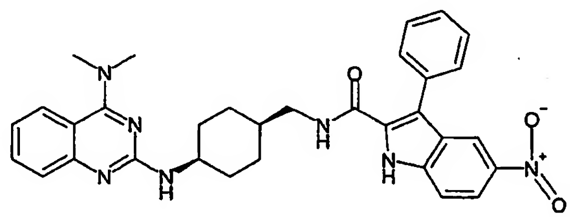
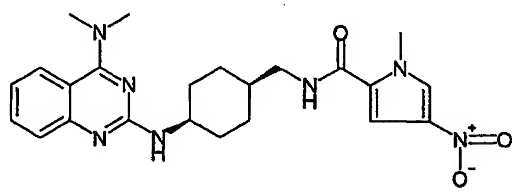
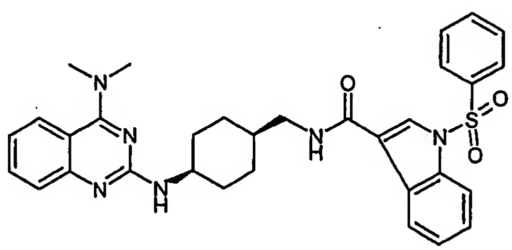
Example No.	Structure	APCI-MS
922		551 (M + H)
923		510 (M + H)
924		522 (M + H)
925		522 (M + H)
926		510 (M + H)

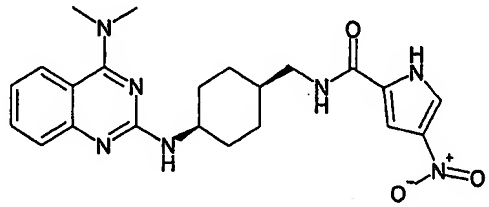
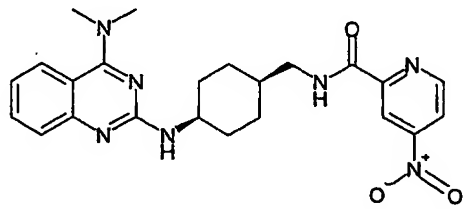
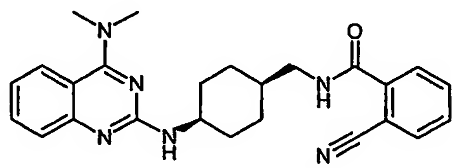
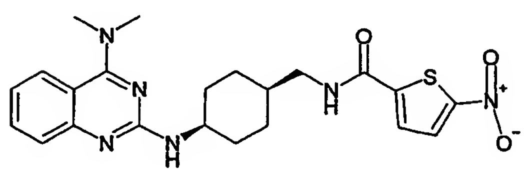
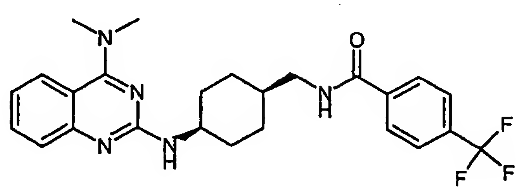
Example No.	Structure	APCI-MS
927		504 (M + H)
928		504 (M + H)
929		578 (M + H)
930		564 (M + H)
931		616 (M + H)

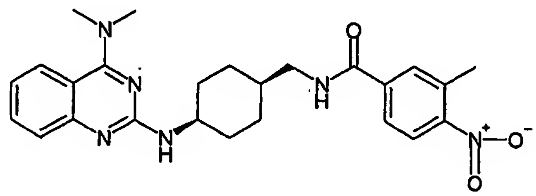
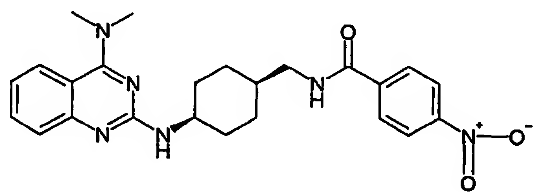
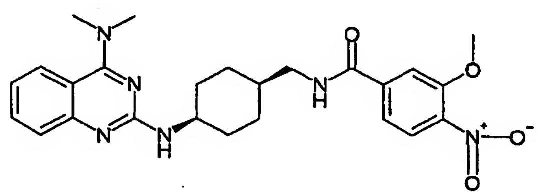
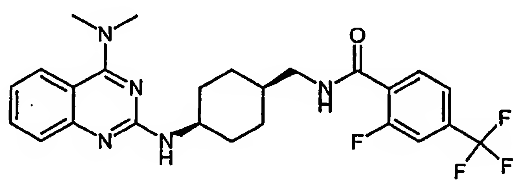
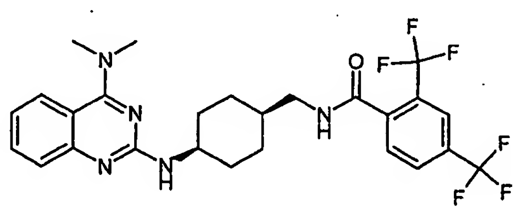
Example No.	Structure	APCI-MS
932		536 (M + H)
933		547 (M + H)
934		482 (M + H)
935		516 (M + H)
936		463 (M + H)

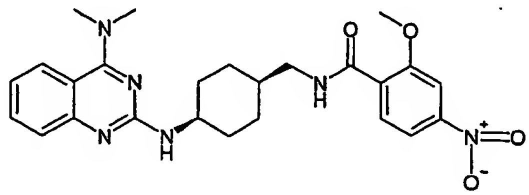
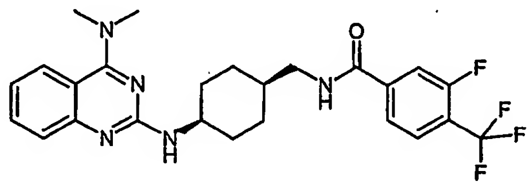
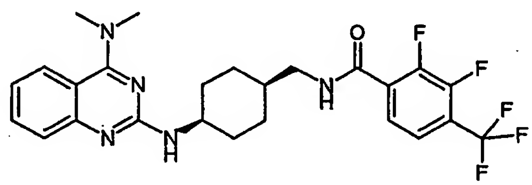
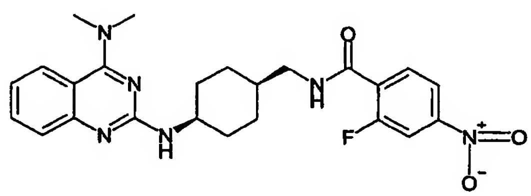
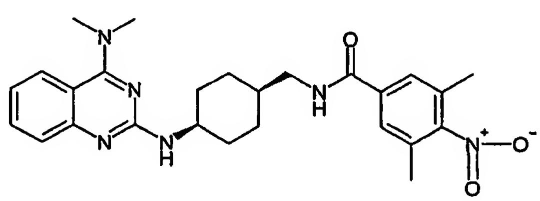
Example No.	Structure	APCI-MS
937		507 (M + H)
938		482 (M + H)
939		515 (M + H)
940		529 (M + H)
941		515 (M + H)

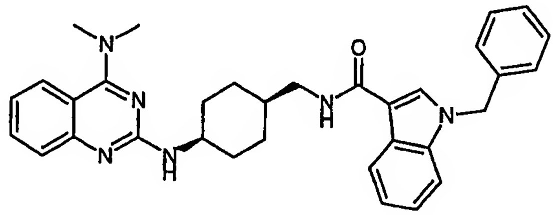
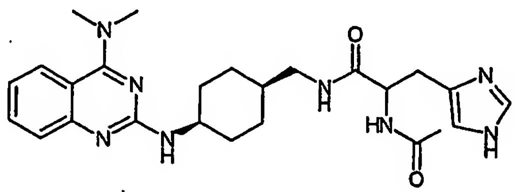
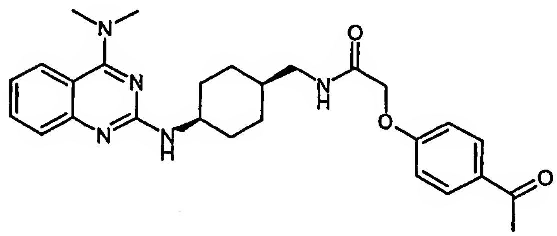
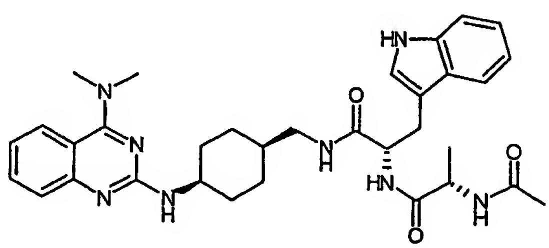
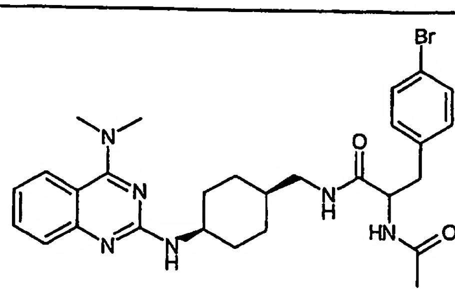
Example No.	Structure	APCI-MS
942		452 (M + H)
943		522 (M + H)
944		596 (M + H)
945		688 (M + H)
946		488 (M + H)

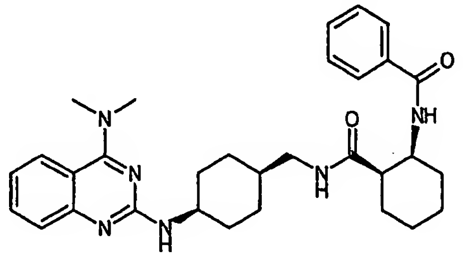
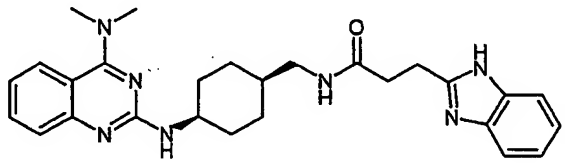
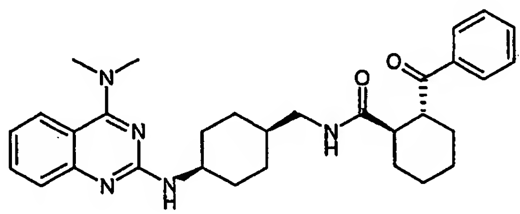
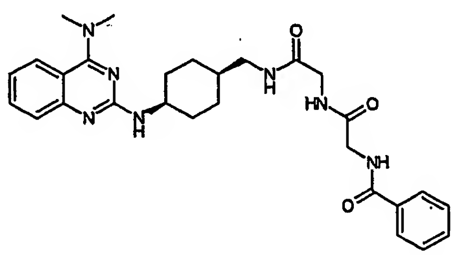
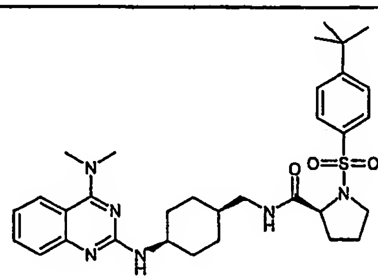
Example No.	Structure	APCI-MS
947		471 (M + H)
948		455 (M + H)
949		564 (M + H)
950		452 (M + H)
951		583 (M + H)

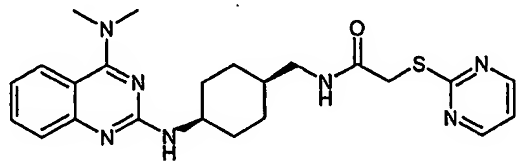
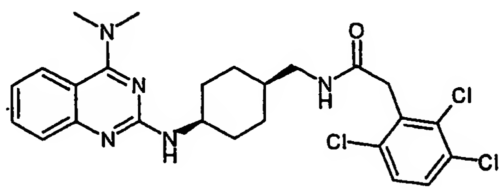
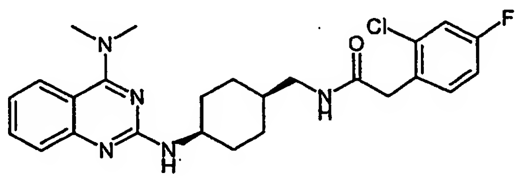
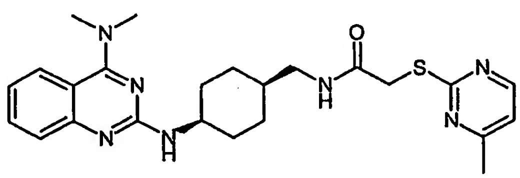
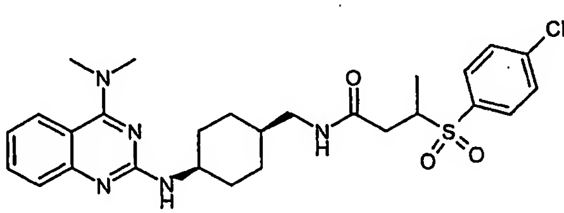
Example No.	Structure	APCI-MS
952		438 (M + H)
953		450 (M + H)
954		429 (M + H)
955		455 (M + H)
956		472 (M + H)

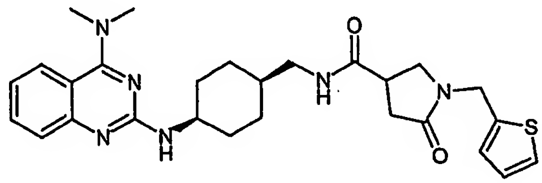
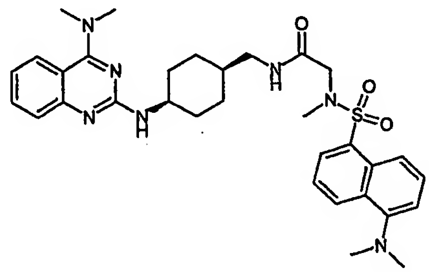
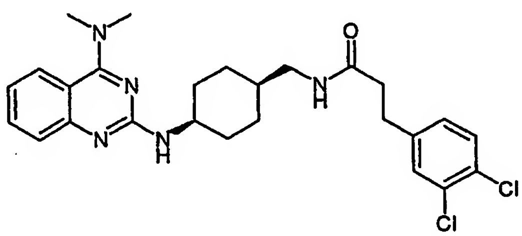
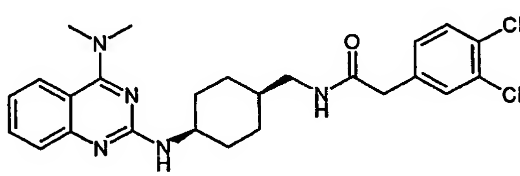
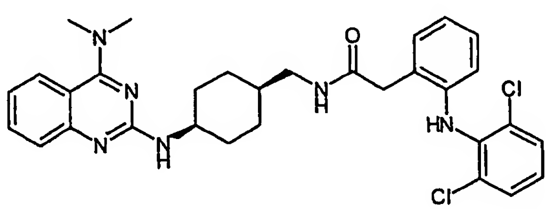
Example No.	Structure	APCI-MS
957		463 (M + H)
958		449 (M + H)
959		479 (M + H)
960		490 (M + H)
961		540 (M + H)

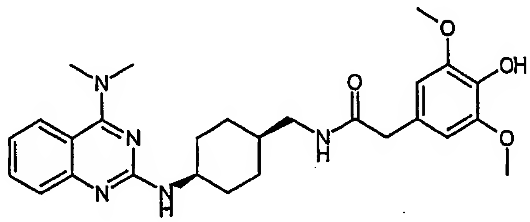
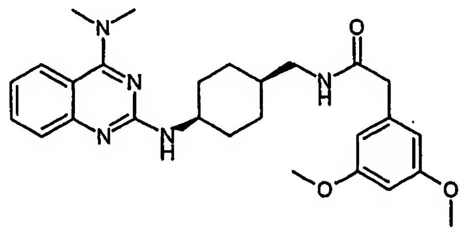
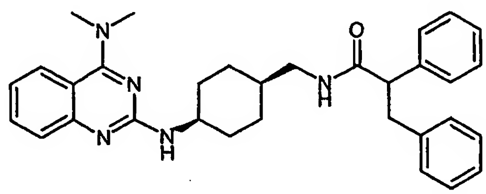
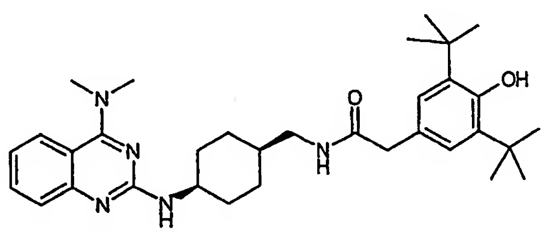
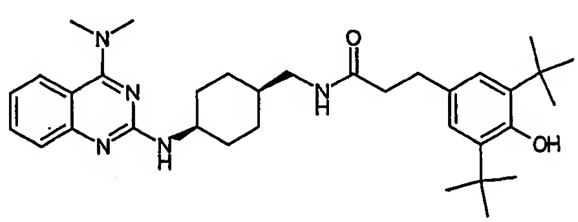
Example No.	Structure	APCI-MS
962		479 (M + H)
963		490 (M + H)
964		508 (M + H)
965		467 (M + H)
966		477 (M + H)

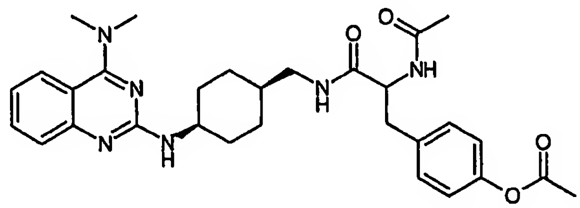
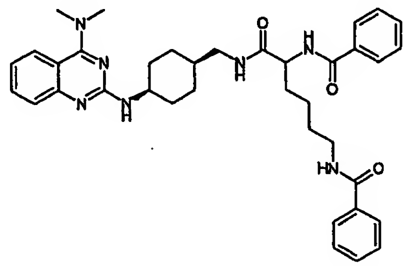
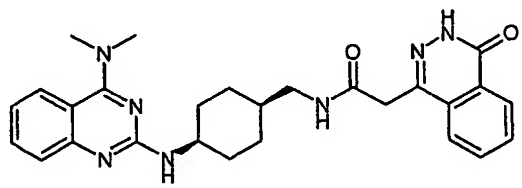
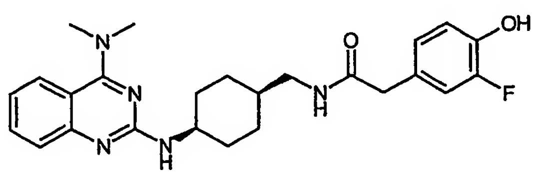
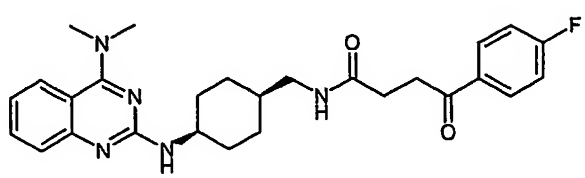
Example No.	Structure	APCI-MS
967		533 (M + H)
968		479 (M + H)
969		476 (M + H)
970		599 (M + H)
971		567 (M + H)

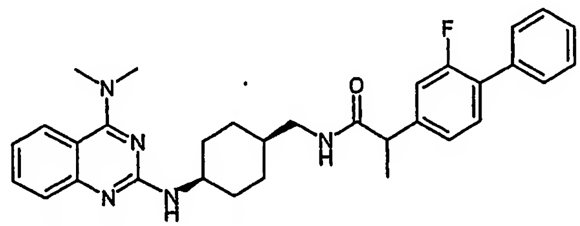
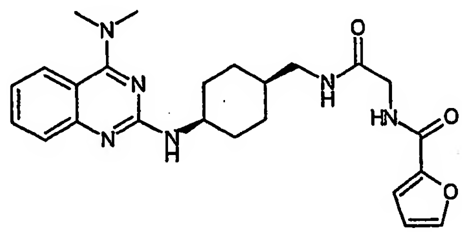
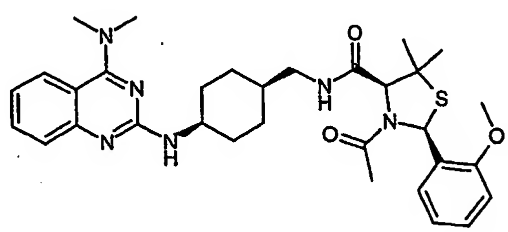
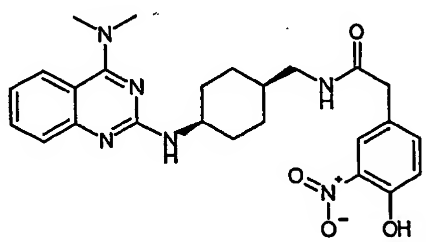
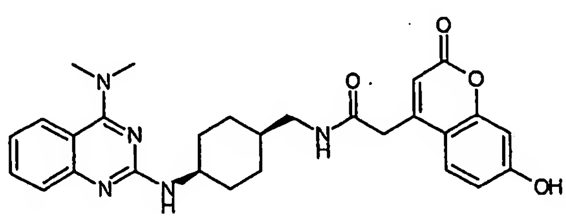
Example No.	Structure	APCI-MS
972		529 (M + H)
973		472 (M + H)
974		514 (M + H)
975		518 (M + H)
976		593 (M + H)

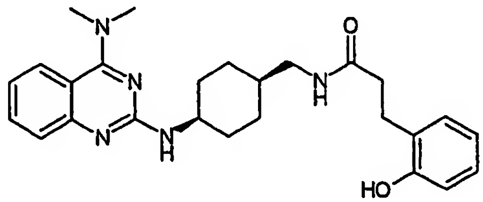
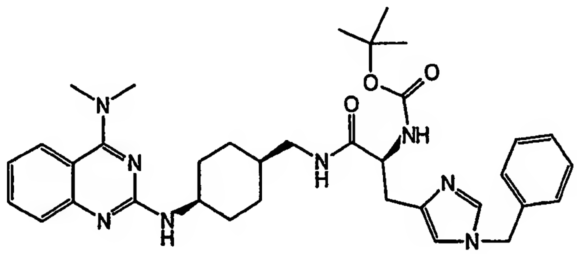
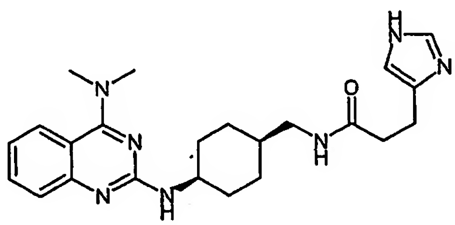
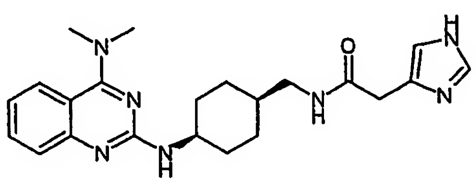
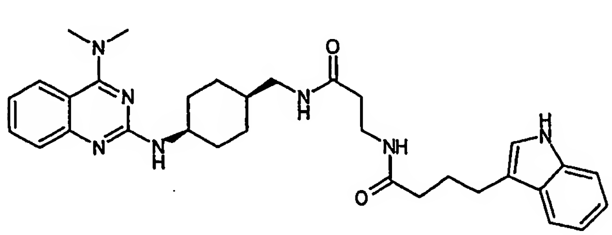
Example No.	Structure	APCI-MS
977		452 (M + H)
978		520 (M + H)
979		470 (M + H)
980		466 (M + H)
981		544 (M + H)

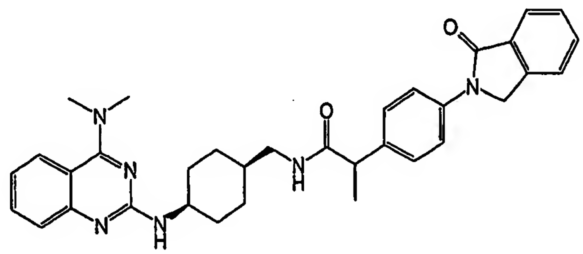
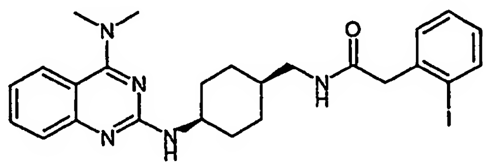
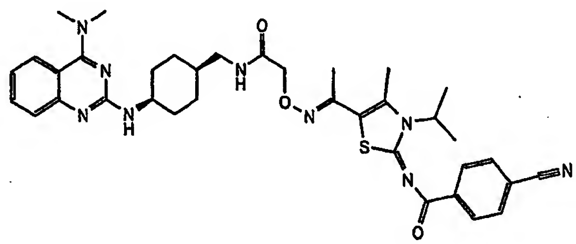
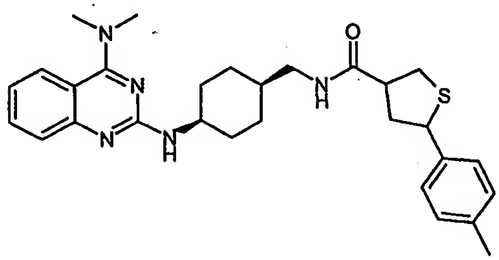
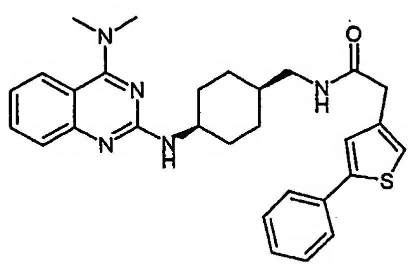
Example No.	Structure	APCI-MS
982		507 (M + H)
983		604 (M + H)
984		500 (M + H)
985		486 (M + H)
986		577 (M + H)

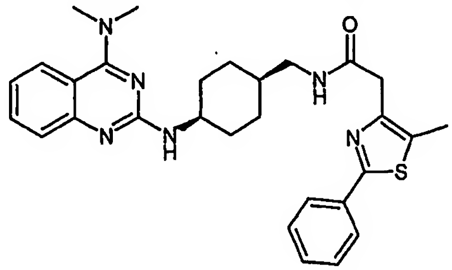
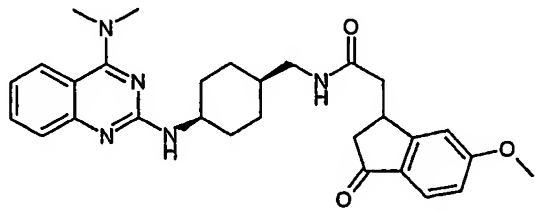
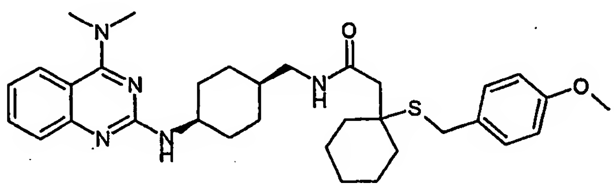
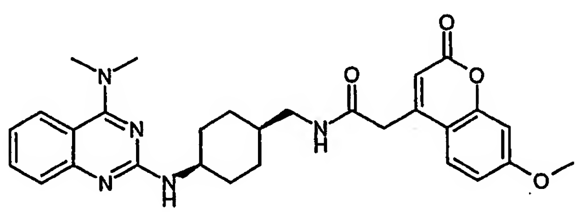
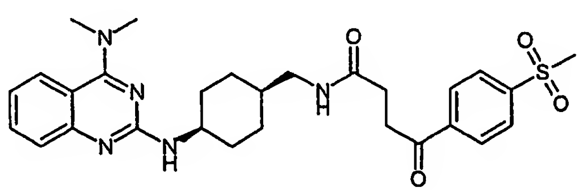
Example No.	Structure	APCI-MS
987		494 (M + H)
988		478 (M + H)
989		508 (M + H)
990		546 (M + H)
991		560 (M + H)

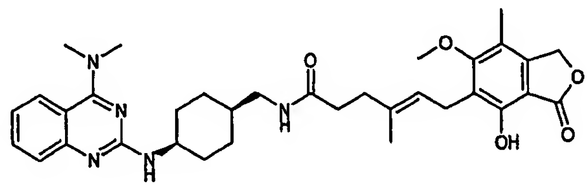
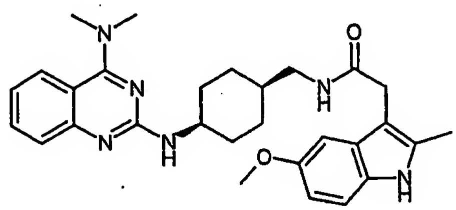
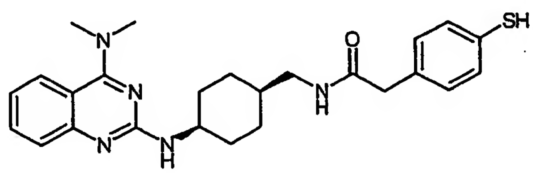
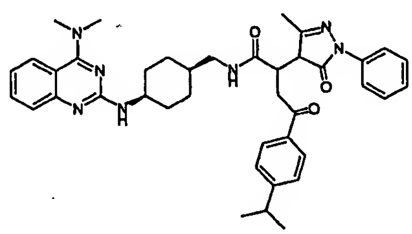
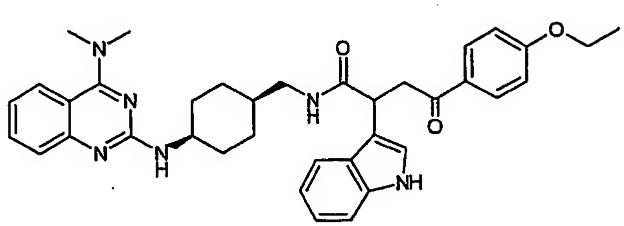
Example No.	Structure	APCI-MS
992		547 (M + H)
993		636 (M + H)
994		486 (M + H)
995		452 (M + H)
996		478 (M + H)

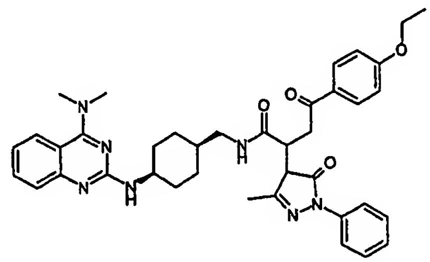
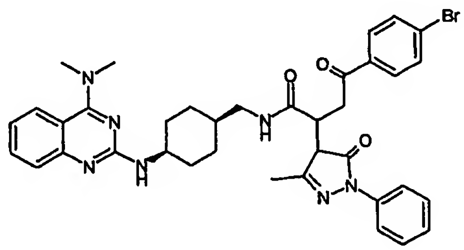
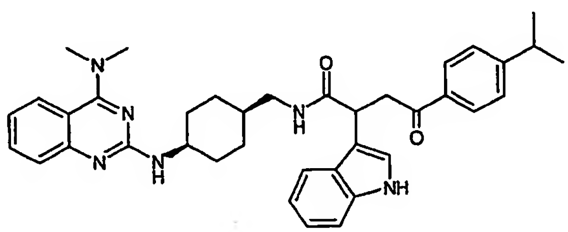
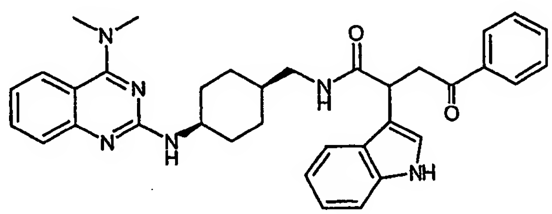
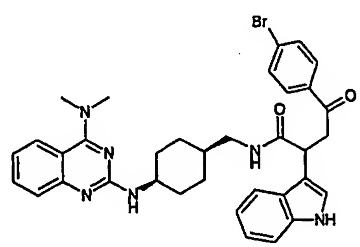
Example No.	Structure	APCI-MS
997		526 (M + H)
998		451 (M + H)
999		591 (M + H)
1000		479 (M + H)
1001		502 (M + H)

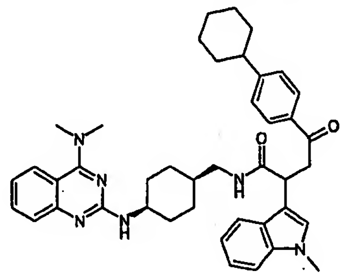
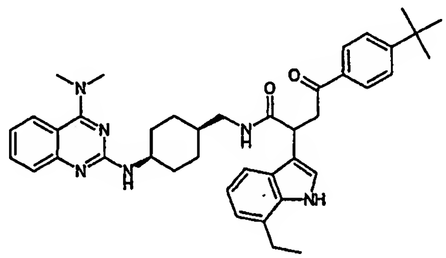
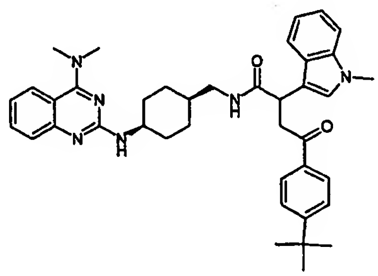
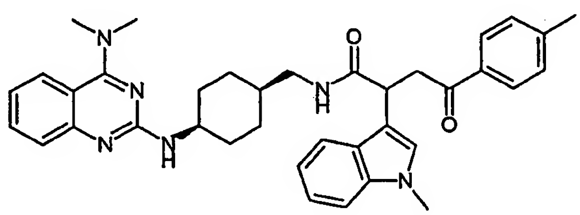
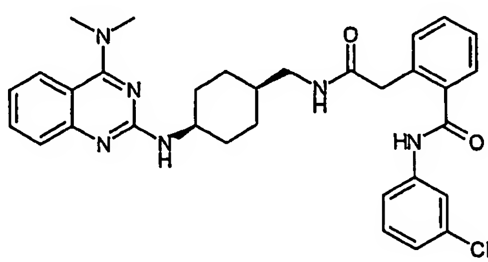
Example No.	Structure	APCI-MS
1002		448 (M + H)
1003		627 (M + H)
1004		422 (M + H)
1005		408 (M + H)
1006		556 (M + H)

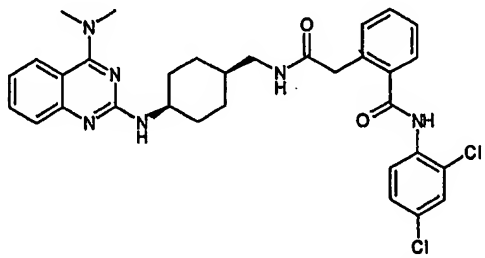
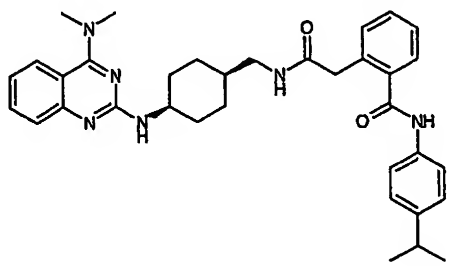
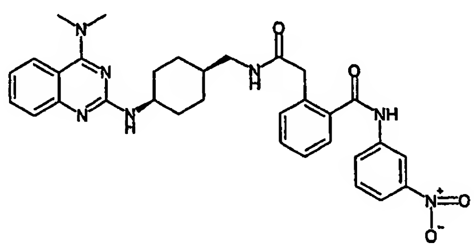
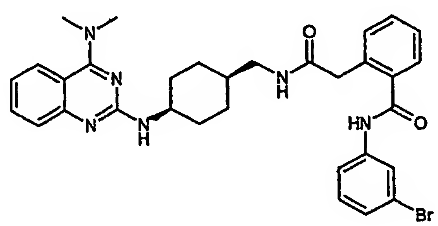
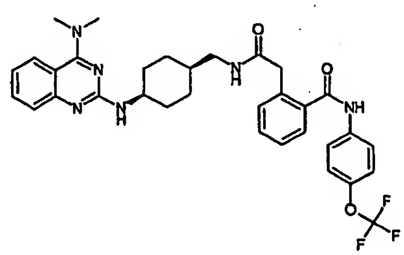
Example No.	Structure	APCI-MS
1007		563 (M + H)
1008		544 (M + H)
1009		682 (M + H)
1010		504 (M + H)
1011		500 (M + H)

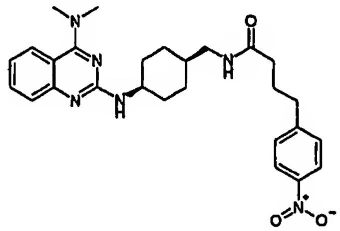
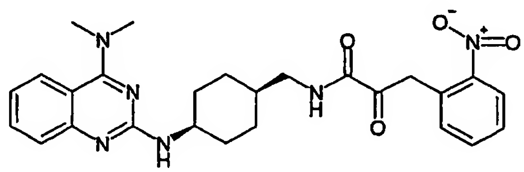
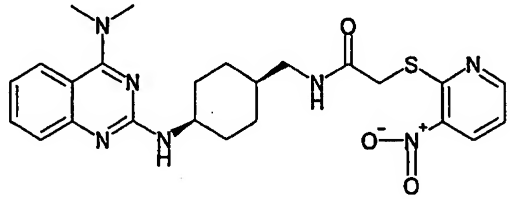
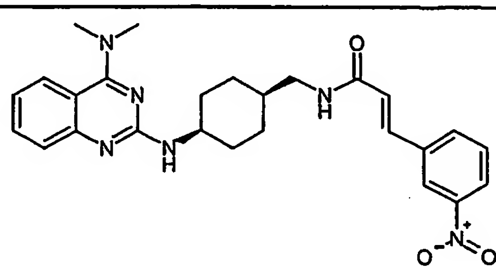
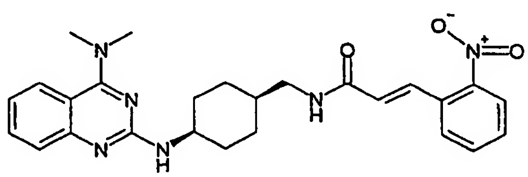
Example No.	Structure	APCI-MS
1012		515 (M + H)
1013		502 (M + H)
1014		576 (M + H)
1015		516 (M + H)
1016		538 (M + H)

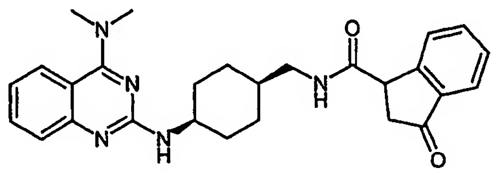
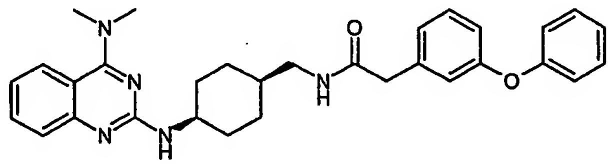
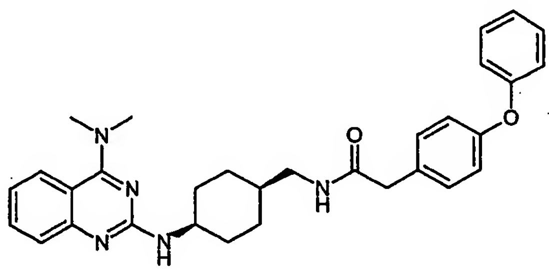
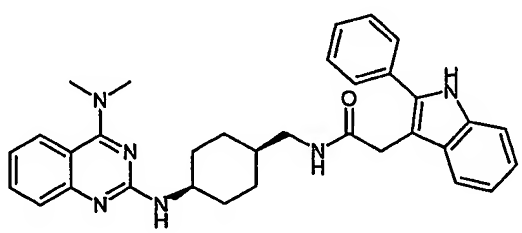
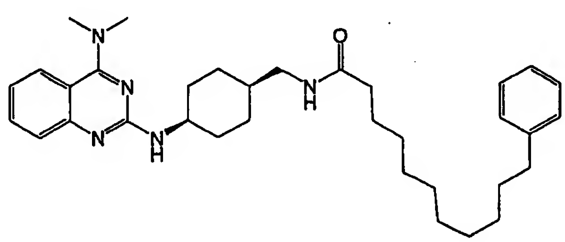
Example No.	Structure	APCI-MS
1017		602 (M + H)
1018		501 (M + H)
1019		450 (M + H)
1020		674 (M + H)
1021		619 (M + H)

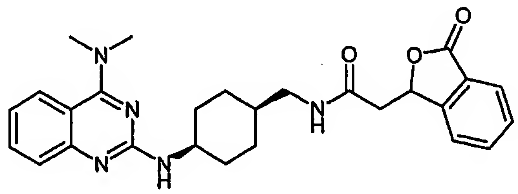
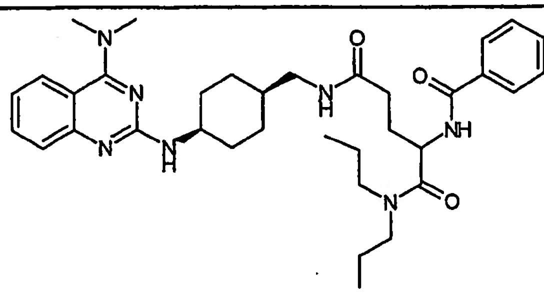
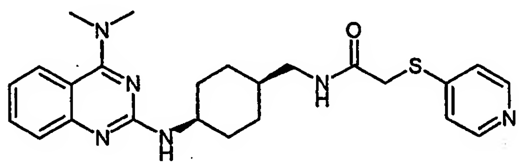
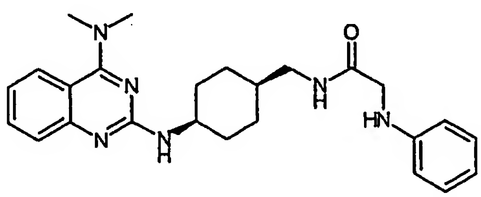
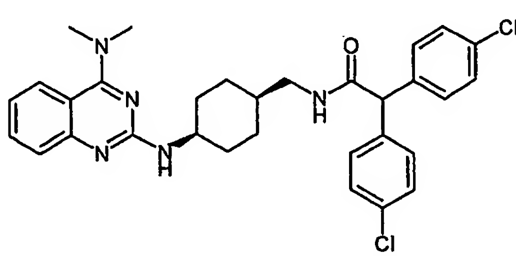
Example No.	Structure	APCI-MS
1022		676 (M + H)
1023		710 (M + H)
1024		617 (M + H)
1025		575 (M + H)
1026		653 (M + H)

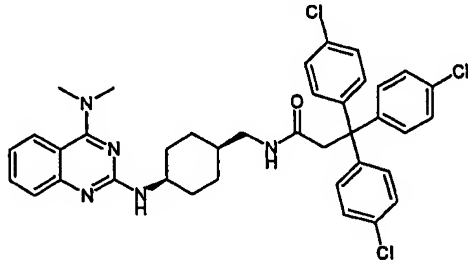
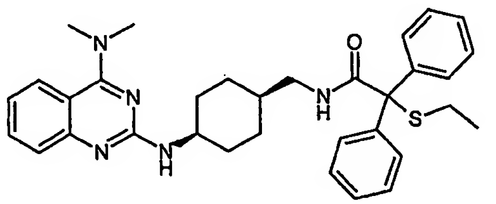
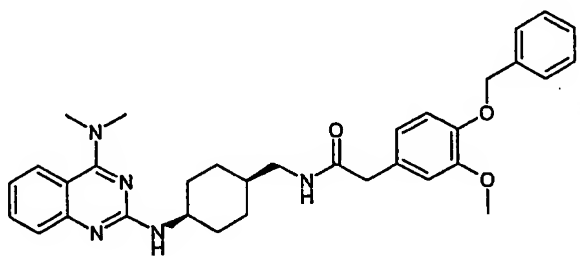
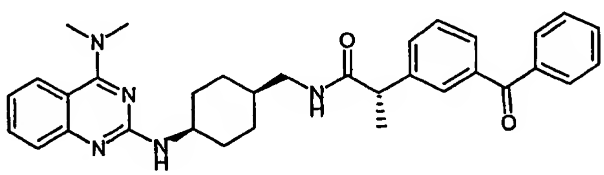
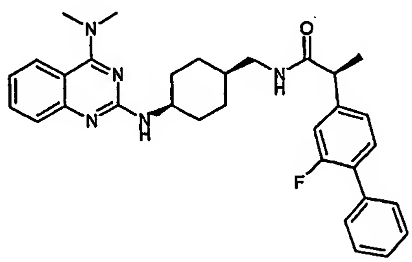
Example No.	Structure	APCI-MS
1027		671 (M + H)
1028		659 (M + H)
1029		645 (M + H)
1030		603 (M + H)
1031		571 (M + H)

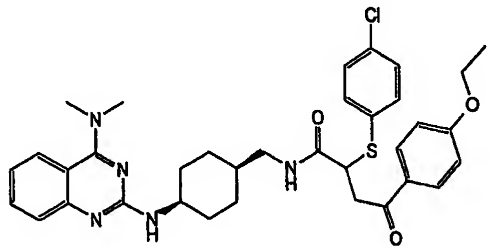
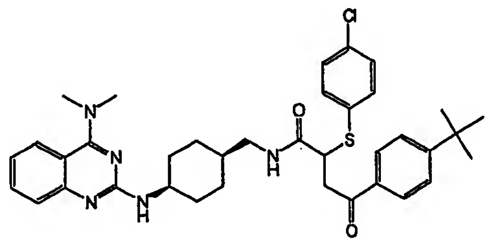
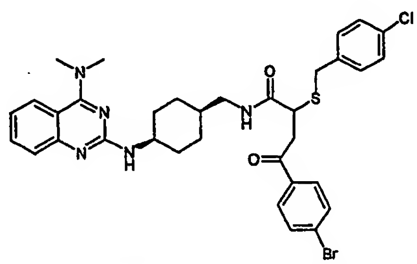
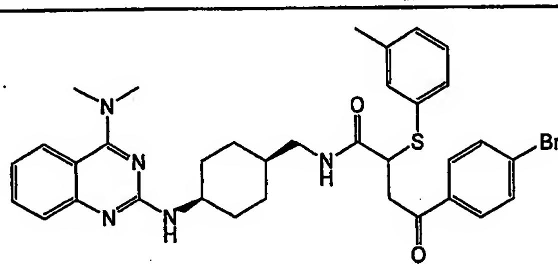
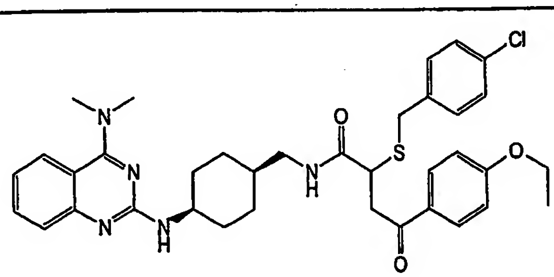
Example No.	Structure	APCI-MS
1032		605 (M + H)
1033		579 (M + H)
1034		582 (M + H)
1035		615 (M + H)
1036		621 (M + H)

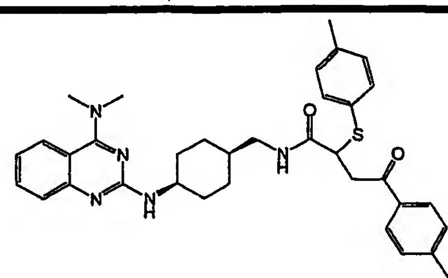
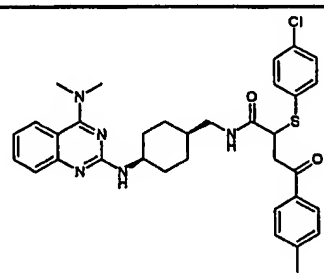
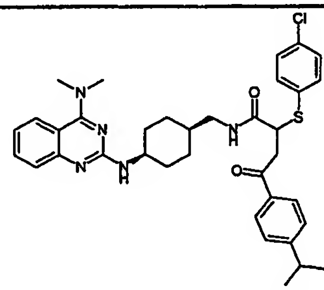
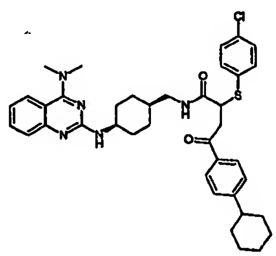
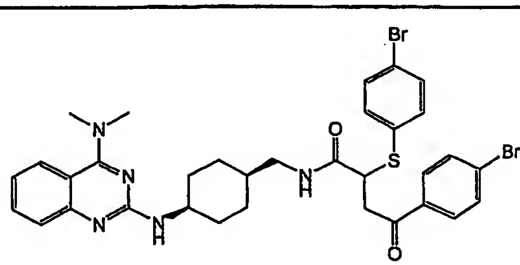
Example No.	Structure	APCI-MS
1037		491 (M + H)
1038		491 (M + H)
1039		496 (M + H)
1040		475 (M + H)
1041		475 (M + H)

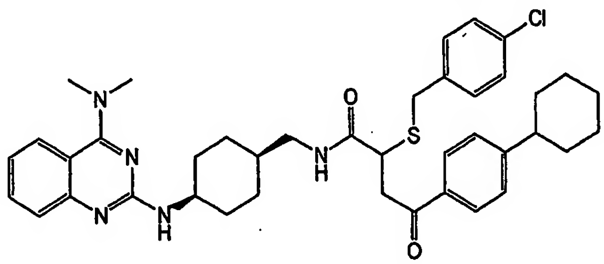
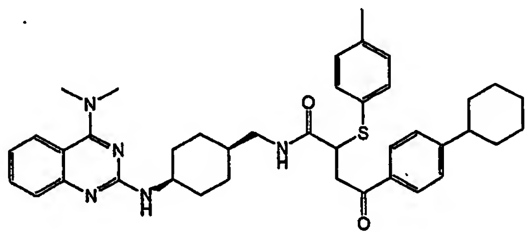
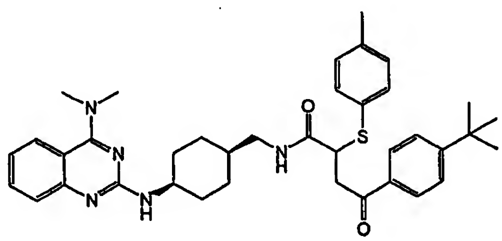
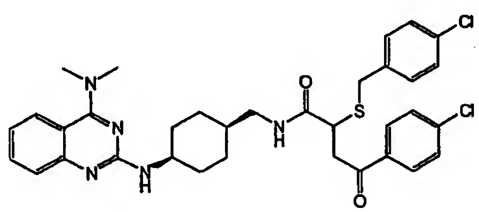
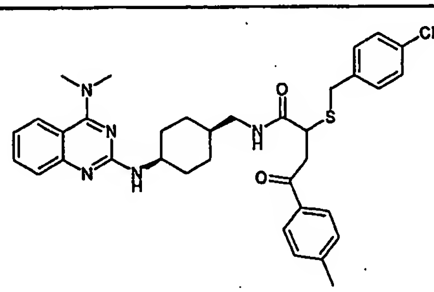
Example No.	Structure	APCI-MS
1042		458 (M + H)
1043		510 (M + H)
1044		510 (M + H)
1045		533 (M + H)
1046		544 (M + H)

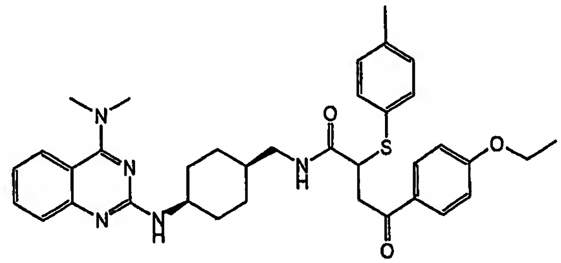
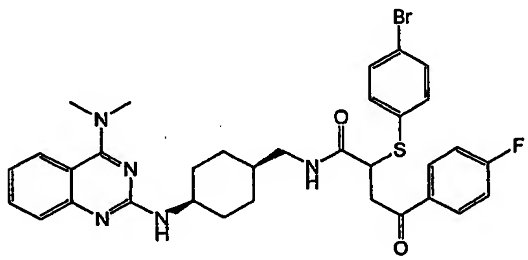
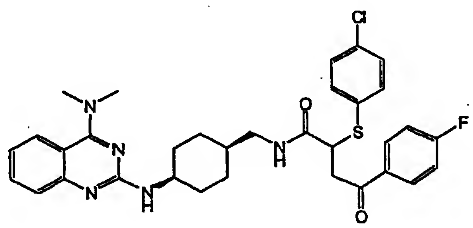
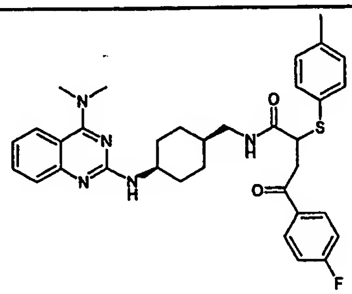
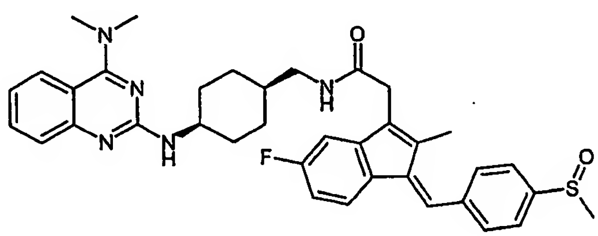
Example No.	Structure	APCI-MS
1047		474 (M + H)
1048		616 (M + H)
1049		451 (M + H)
1050		433 (M + H)
1051		562 (M + H)

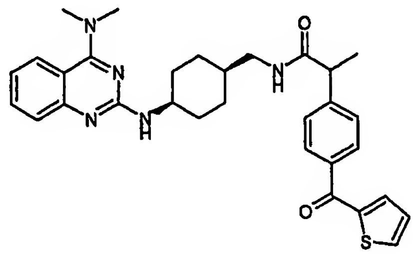
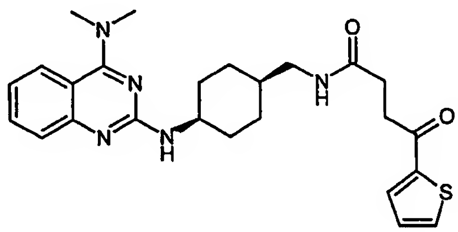
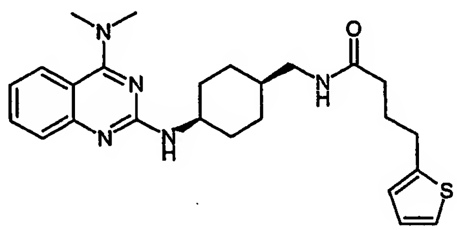
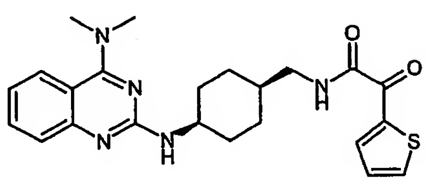
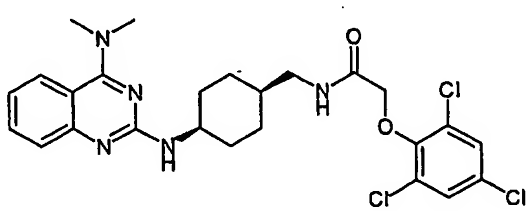
Example No.	Structure	APCI-MS
1052		686 (M + H)
1053		554 (M + H)
1054		554 (M + H)
1055		536 (M + H)
1056		526 (M + H)

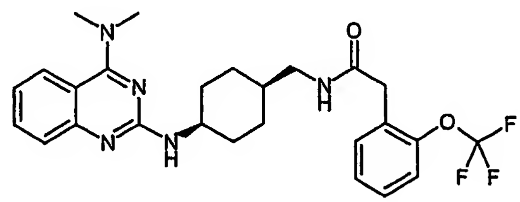
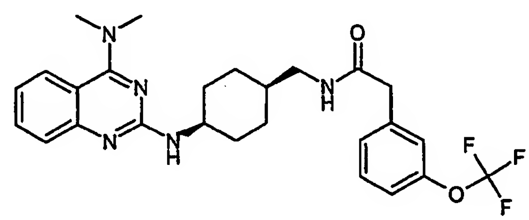
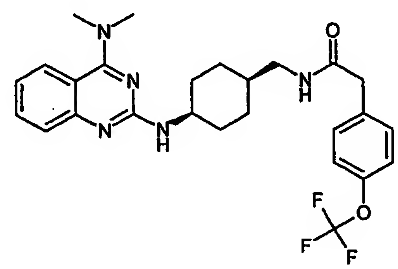
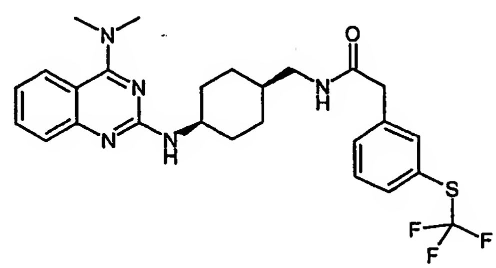
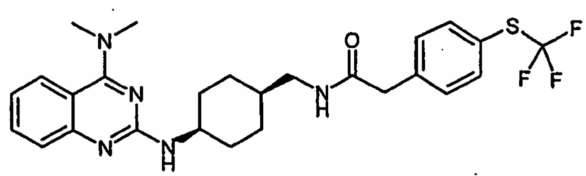
Example No.	Structure	APCI-MS
1057		646 (M + H)
1058		658 (M + H)
1059		694 (M + H)
1060		660 (M + H)
1061		660 (M + H)

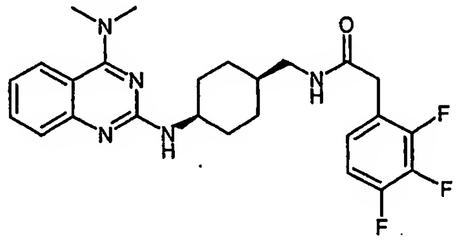
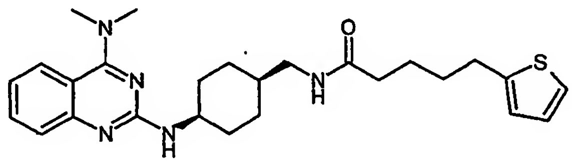
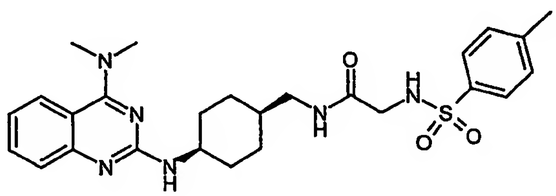
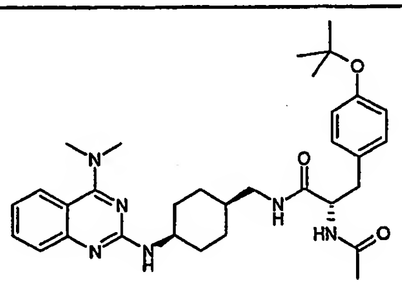
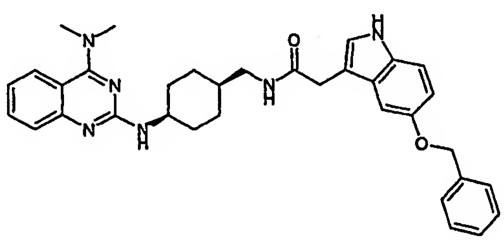
Example No.	Structure	APCI-MS
1062		596 (M + H)
1063		616 (M + H)
1064		644 (M + H)
1065		684 (M + H)
1066		724 (M + H)

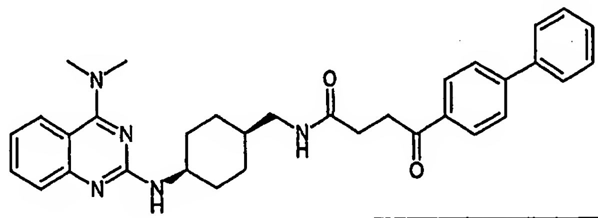
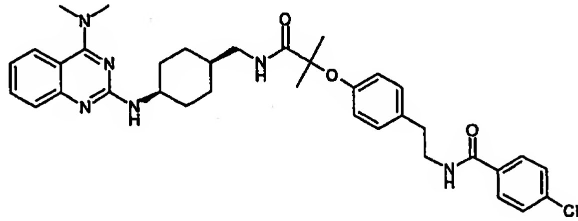
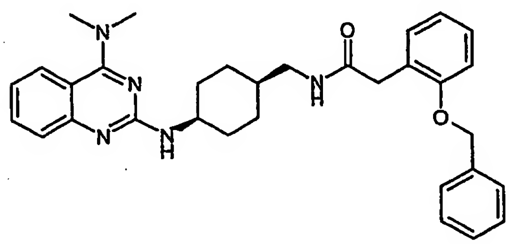
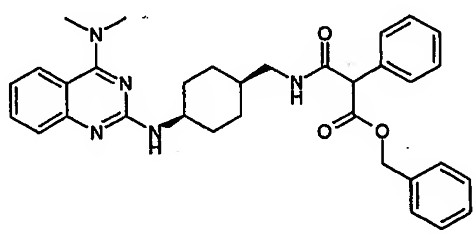
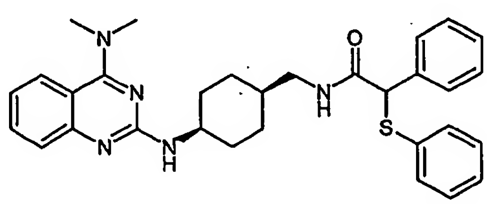
Example No.	Structure	APCI-MS
1067		698 (M + H)
1068		664 (M + H)
1069		638 (M + H)
1070		650 (M + H)
1071		630 (M + H)

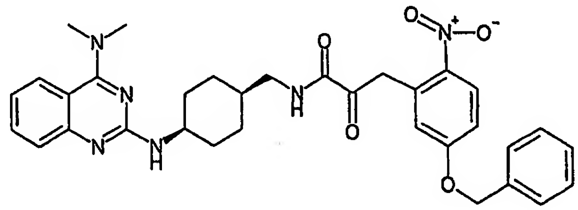
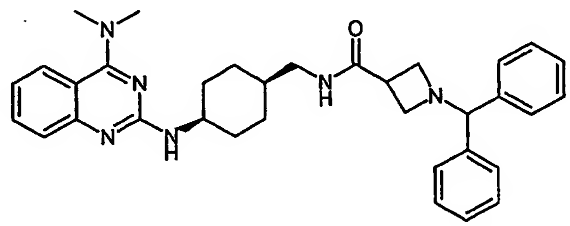
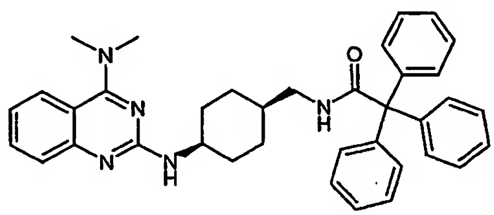
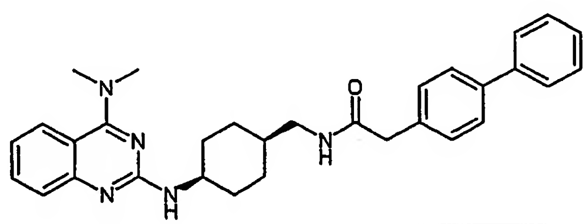
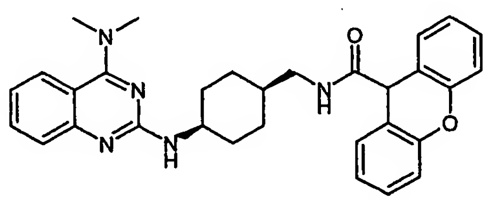
Example No.	Structure	APCI-MS
1072		626 (M + H)
1073		664 (M + H)
1074		620 (M + H)
1075		600 (M + H)
1076		638 (M + H)

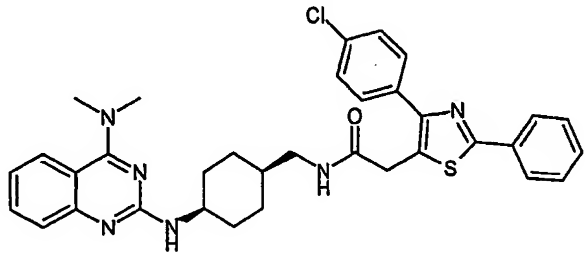
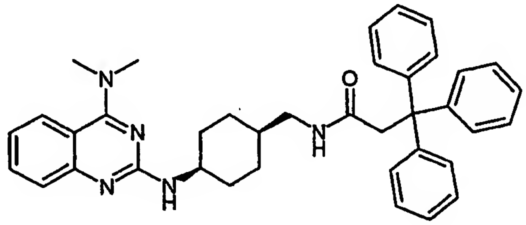
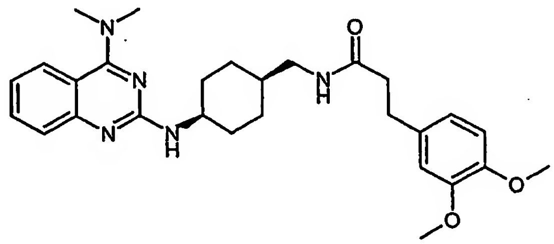
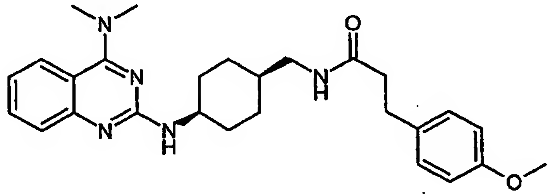
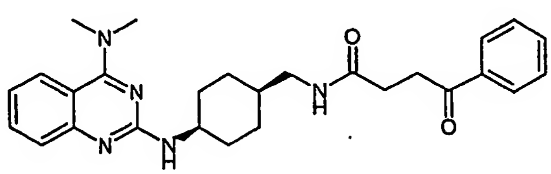
Example No.	Structure	APCI-MS
1077		542 (M + H)
1078		466 (M + H)
1079		452 (M + H)
1080		438 (M + H)
1081		536 (M + H)

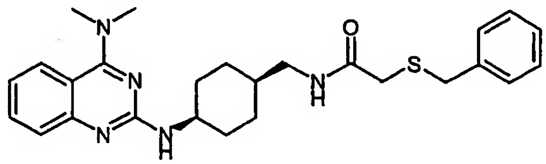
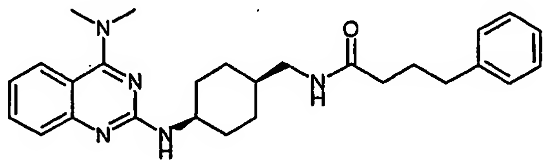
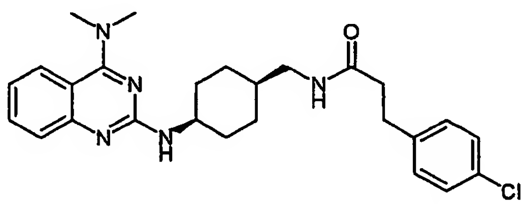
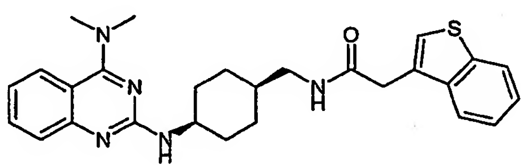
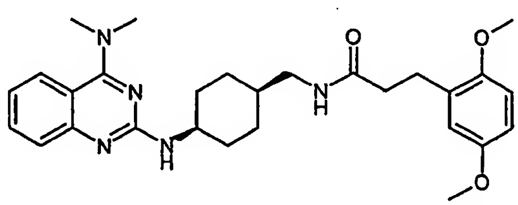
Example No.	Structure	APCI-MS
1082		502 (M + H)
1083		502 (M + H)
1084		502 (M + H)
1085		518 (M + H)
1086		518 (M + H)

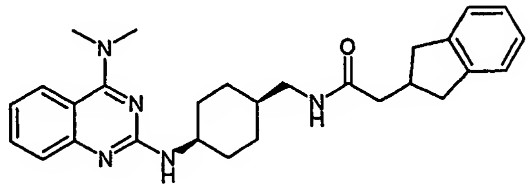
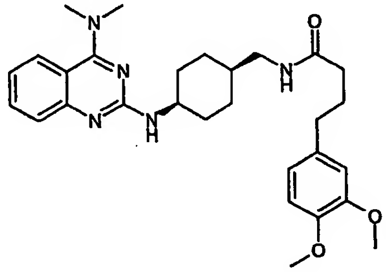
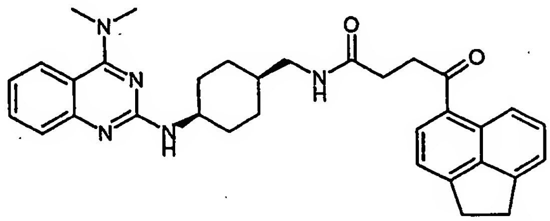
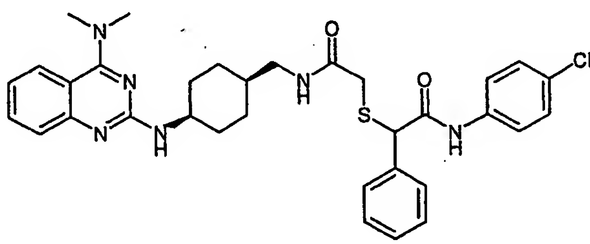
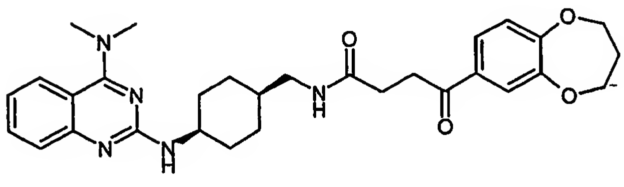
Example No.	Structure	APCI-MS
1087		472 (M + H)
1088		466 (M + H)
1089		511 (M + H)
1090		561 (M + H)
1091		563 (M + H)

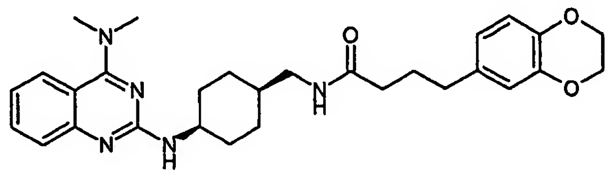
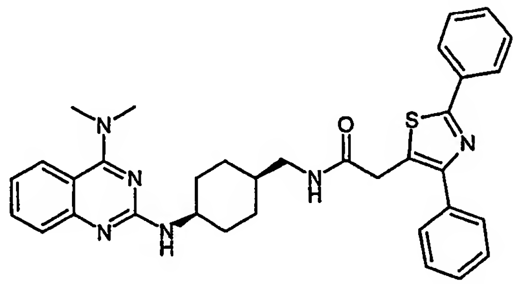
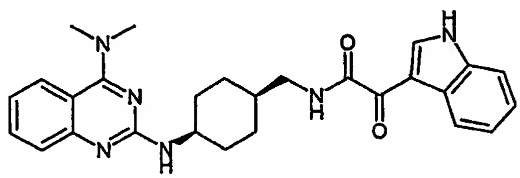
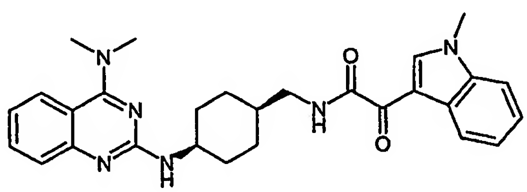
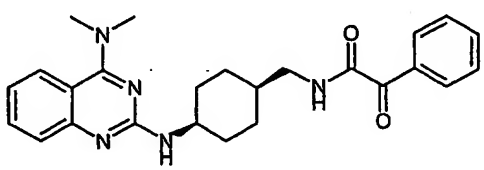
Example No.	Structure	APCI-MS
1092		536 (M+H)
1093		643 (M+H)
1094		524 (M+H)
1095		552 (M+H)
1096		526 (M+H)

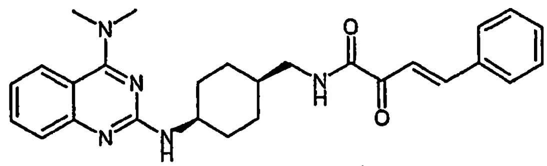
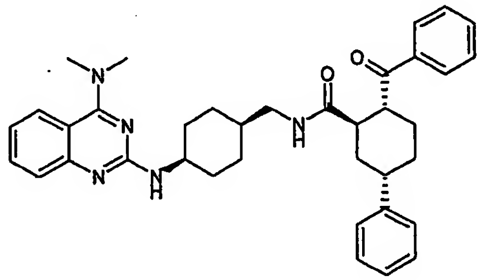
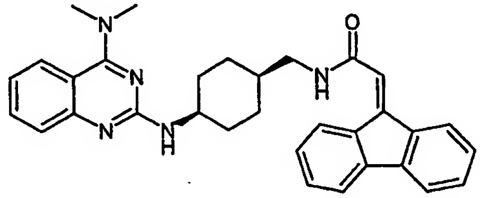
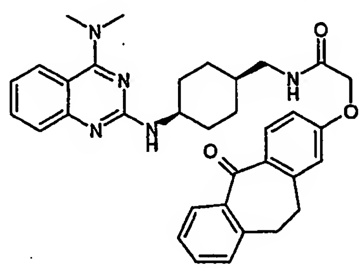
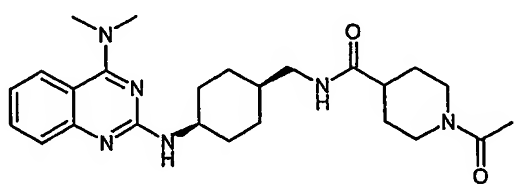
Example No.	Structure	APCI-MS
1097		597 (M + H)
1098		549 (M + H)
1099		570 (M + H)
1100		494 (M + H)
1101		508 (M + H)

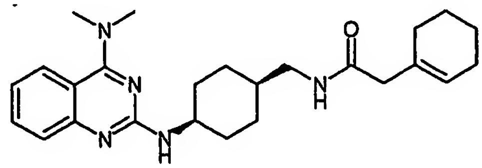
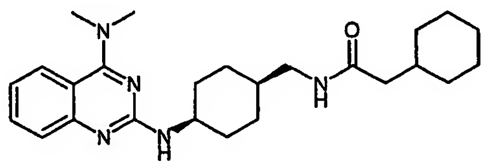
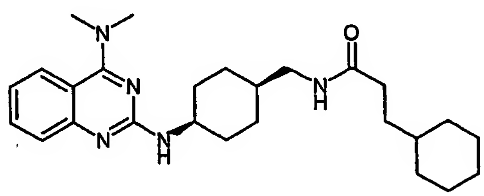
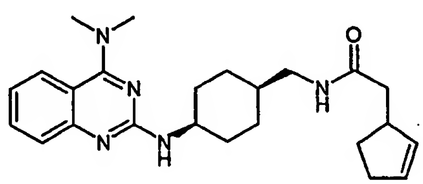
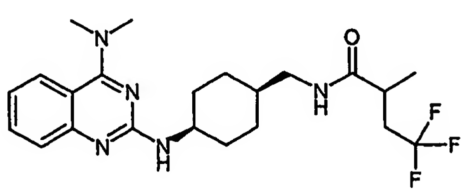
Example No.	Structure	APCI-MS
1102		611 (M + H)
1103		584 (M + H)
1104		492 (M + H)
1105		462 (M + H)
1106		460 (M + H)

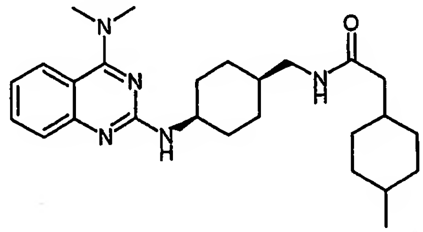
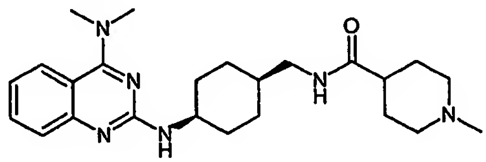
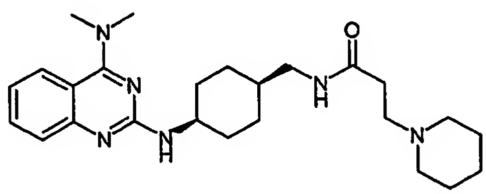
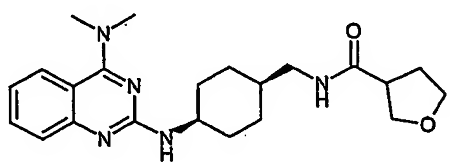
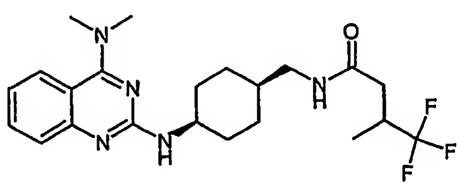
Example No.	Structure	APCI-MS
1107		464 (M + H)
1108		446 (M + H)
1109		466 (M + H)
1110		474 (M + H)
1111		492 (M + H)

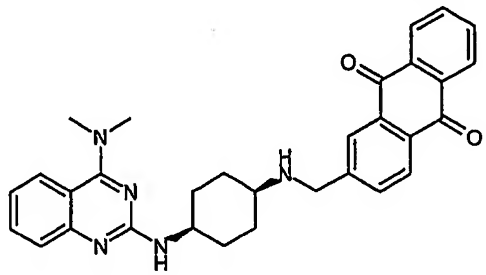
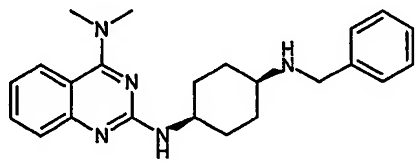
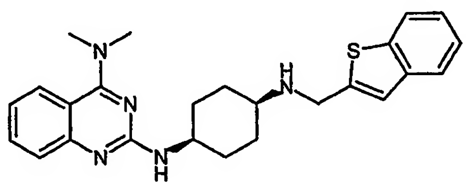
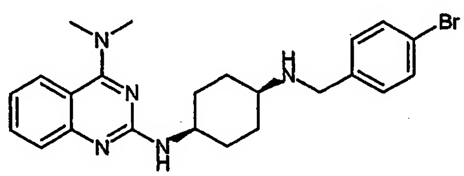
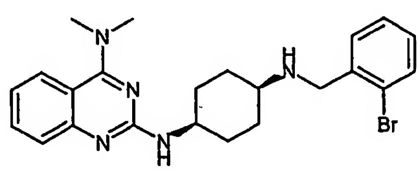
Example No.	Structure	APCI-MS
1112		458 (M + H)
1113		506 (M + H)
1114		536 (M + H)
1115		617 (M + H)
1116		532 (M + H)

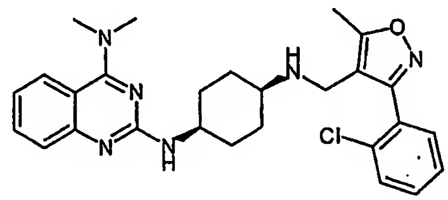
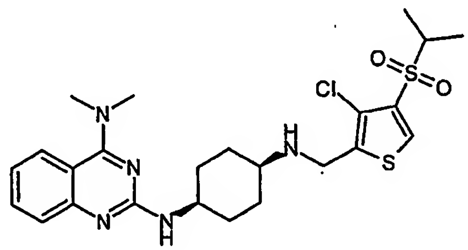
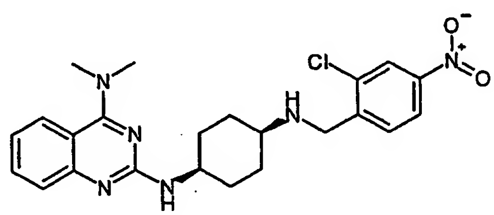
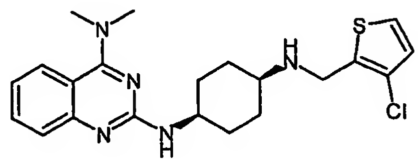
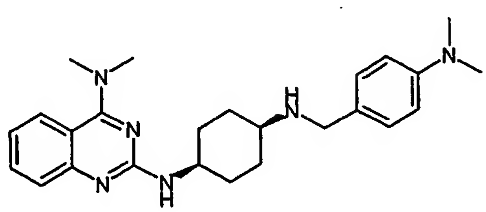
Example No.	Structure	APCI-MS
1117		504 (M + H)
1118		577 (M + H)
1119		471 (M + H)
1120		485 (M + H)
1121		432 (M + H)

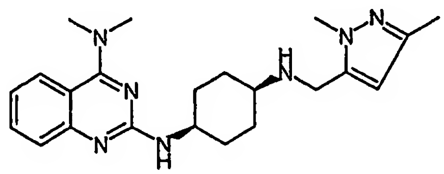
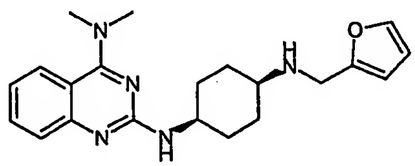
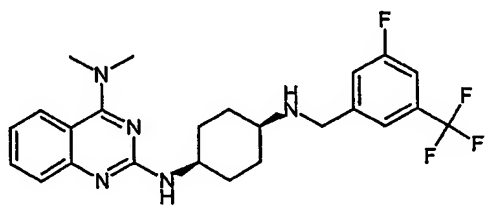
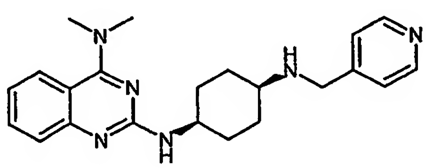
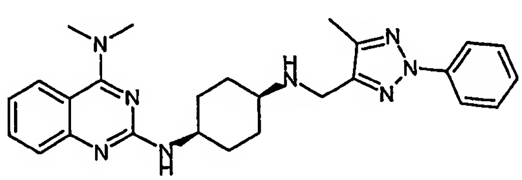
Example No.	Structure	APCI-MS
1122		458 (M + H)
1123		590 (M + H)
1124		504 (M + H)
1125		564 (M + H)
1126		453 (M + H)

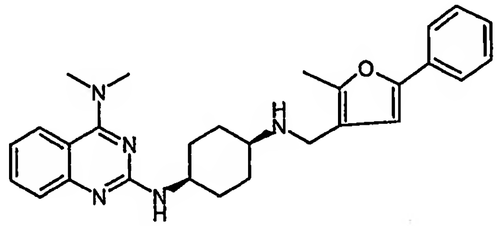
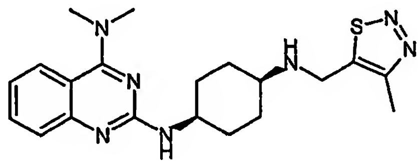
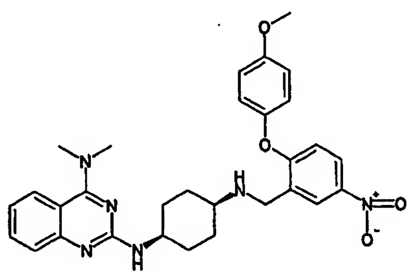
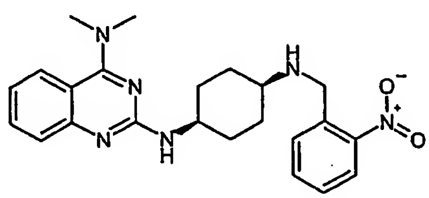
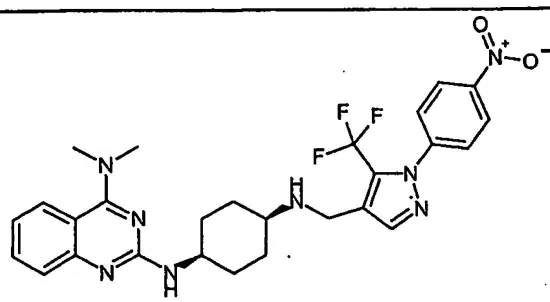
Example No.	Structure	APCI-MS
1127		422 (M + H)
1128		424 (M + H)
1129		438 (M + H)
1130		408 (M + H)
1131		438 (M + H)

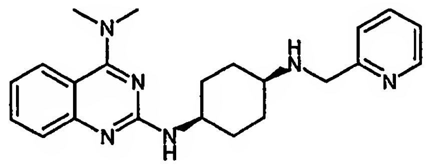
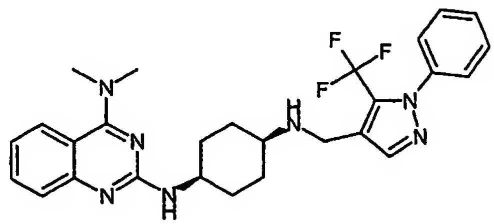
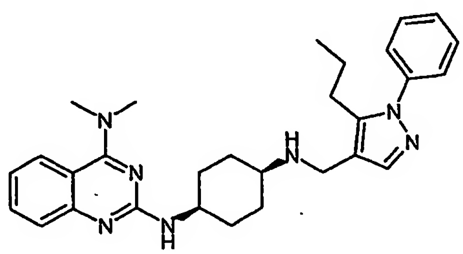
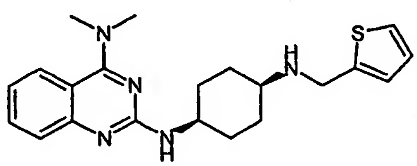
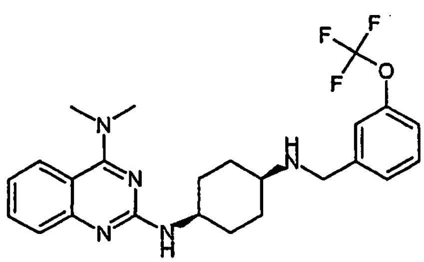
Example No.	Structure	APCI-MS
1132		438 (M + H)
1133		425 (M + H)
1134		439 (M + H)
1135		398 (M + H)
1136		438 (M + H)

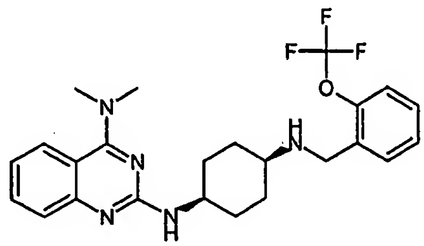
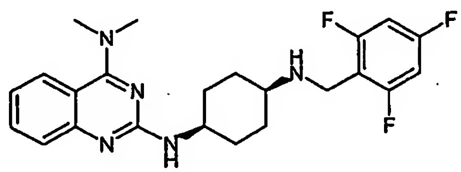
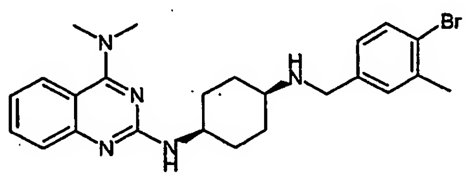
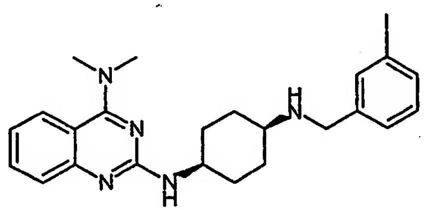
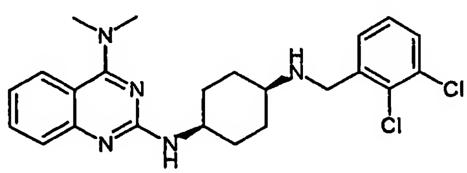
Example No.	Structure	APCI-MS
1137		506 (M + H)
1138		376 (M + H)
1139		432 (M + H)
1140		454 (M + H)
1141		454 (M + H)

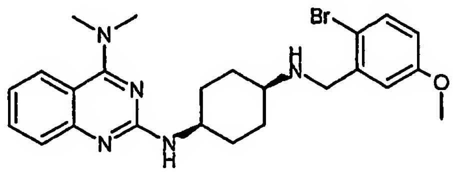
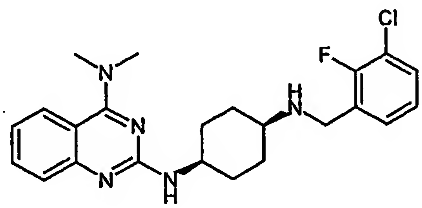
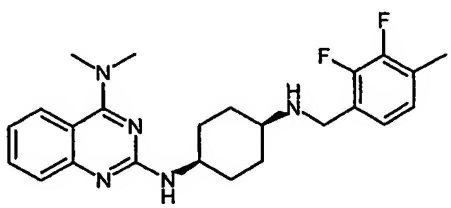
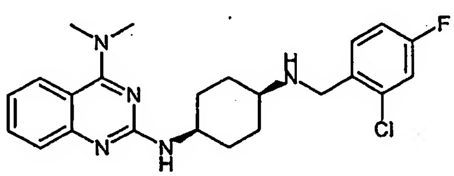
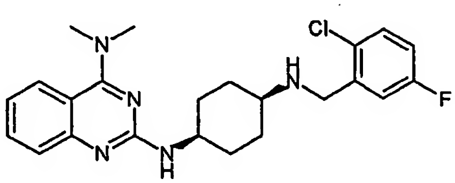
Example No.	Structure	APCI-MS
1142		491 (M + H)
1143		522 (M + H)
1144		455 (M + H)
1145		416 (M + H)
1146		419 (M + H)

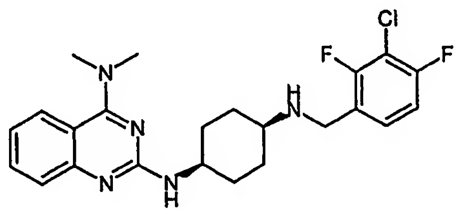
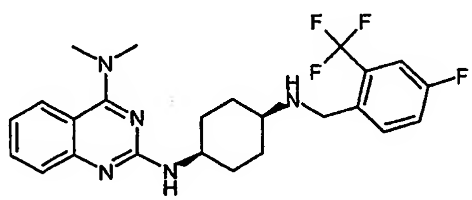
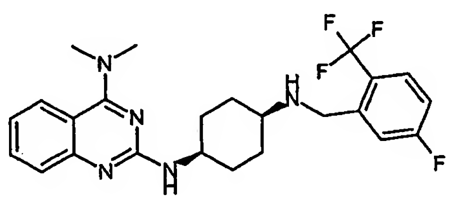
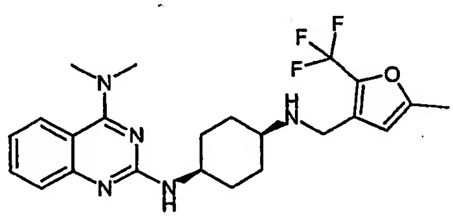
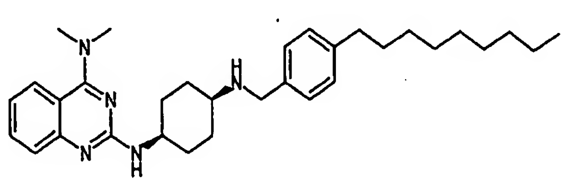
Example No.	Structure	APCI-MS
1147		394 (M + H)
1148		366 (M + H)
1149		462 (M + H)
1150		377 (M + H)
1151		457 (M + H)

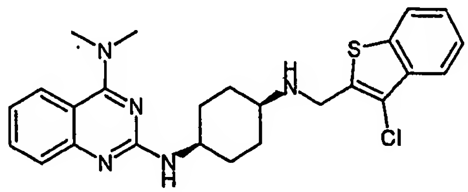
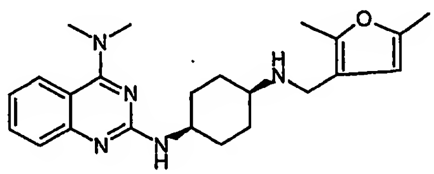
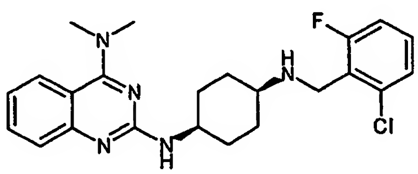
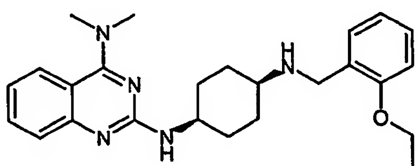
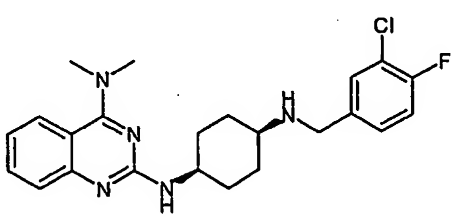
Example No.	Structure	APCI-MS
1152		456 (M + H)
1153		398 (M + H)
1154		543 (M + H)
1155		421 (M + H)
1156		555 (M + H)

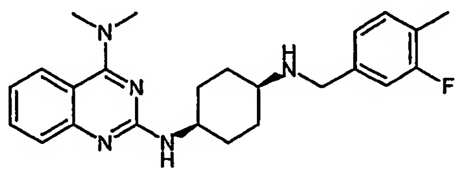
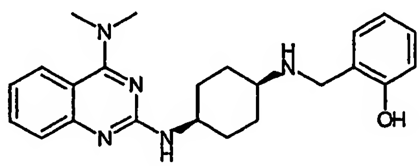
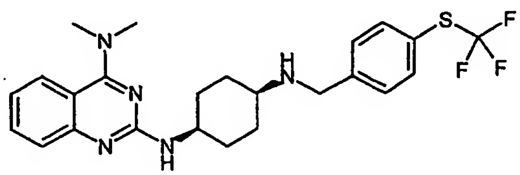
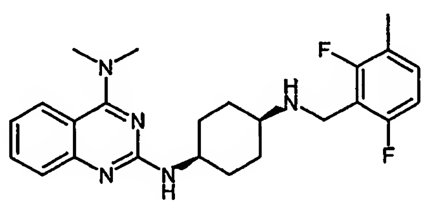
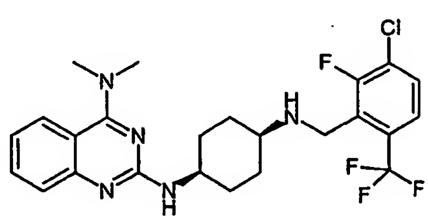
Example No.	Structure	APCI-MS
1157		377 (M + H)
1158		510 (M + H)
1159		484 (M + H)
1160		382 (M + H)
1161		460 (M + H)

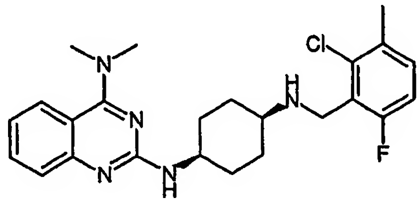
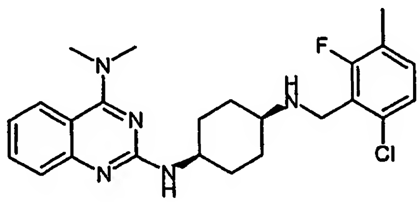
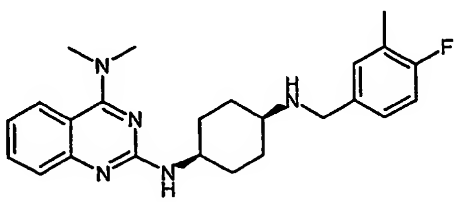
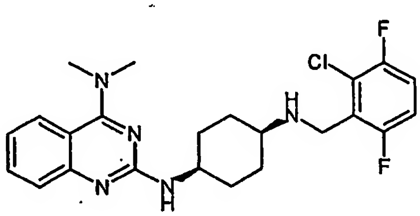
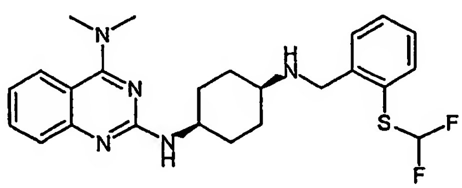
Example No.	Structure	APCI-MS
1162		460 (M + H)
1163		430 (M + H)
1164		468 (M + H)
1165		502 (M + H)
1166		444 (M + H)

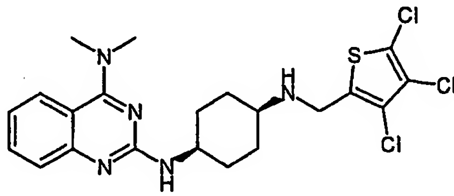
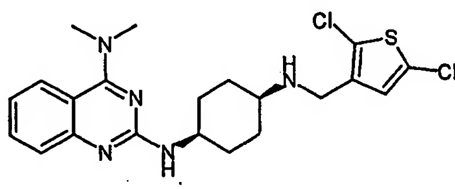
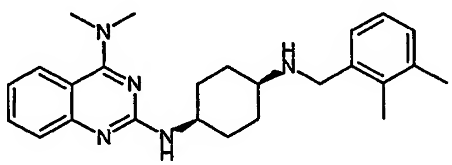
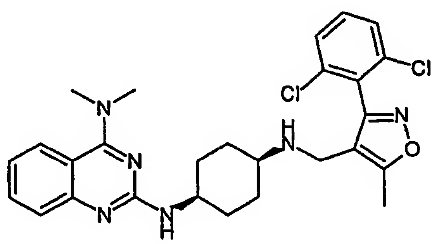
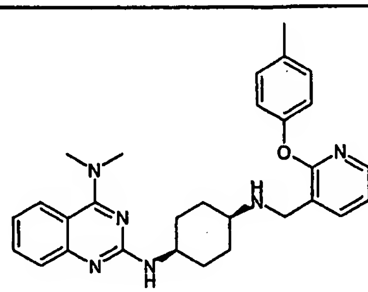
Example No.	Structure	APCI-MS
1167		484 (M + H)
1168		428 (M + H)
1169		426 (M + H)
1170		428 (M + H)
1171		428 (M + H)

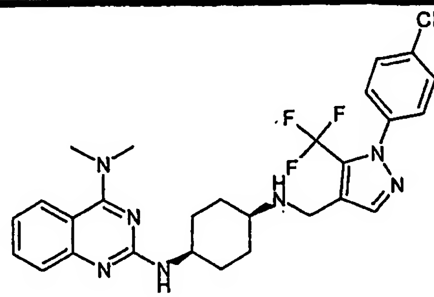
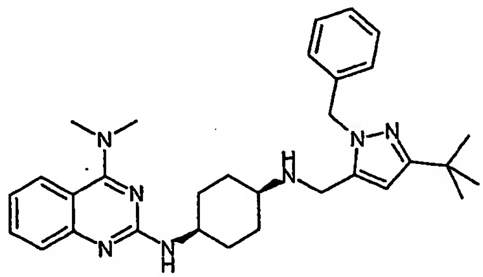
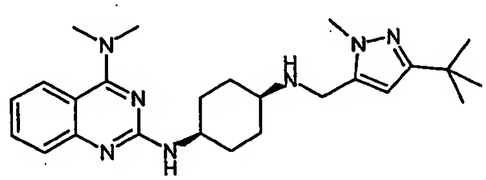
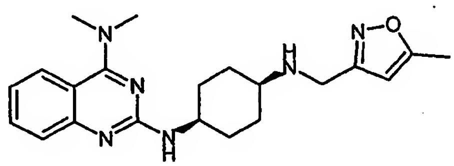
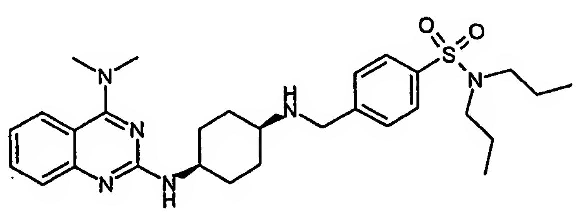
Example No.	Structure	APCI-MS
1172		446 (M + H)
1173		462 (M + H)
1174		462 (M + H)
1175		448 (M + H)
1176		502 (M + H)

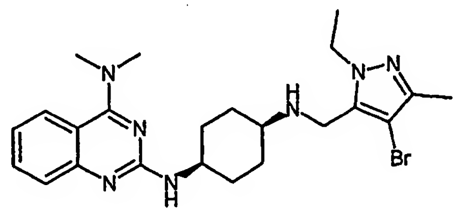
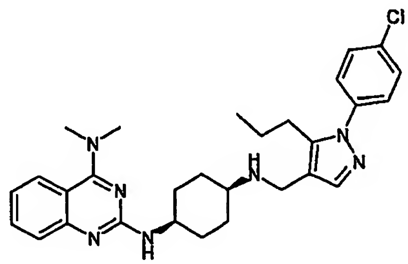
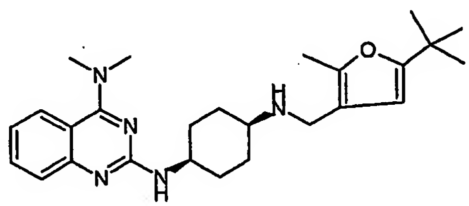
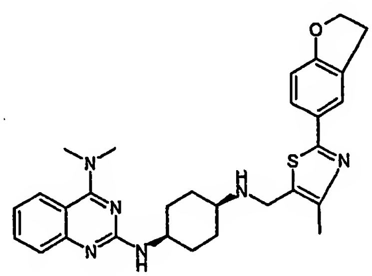
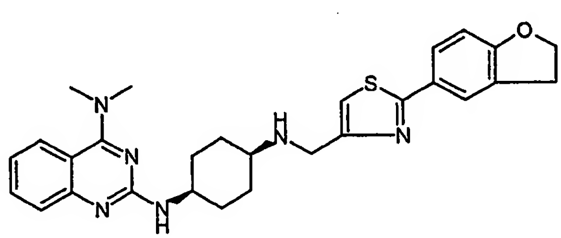
Example No.	Structure	APCI-MS
1177		466 (M + H)
1178		394 (M + H)
1179		428 (M + H)
1180		420 (M + H)
1181		428 (M + H)

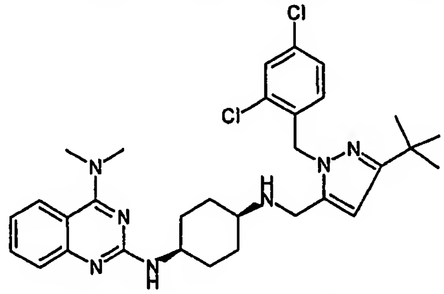
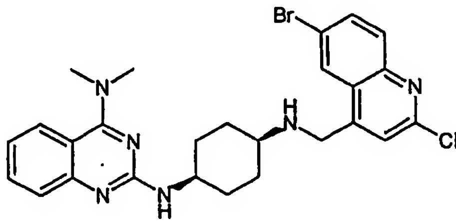
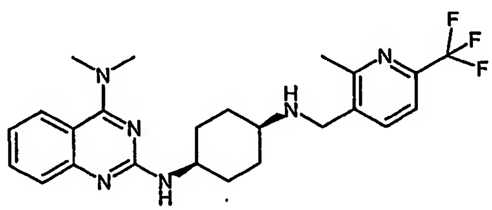
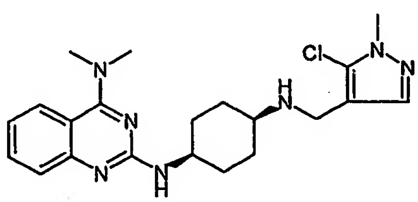
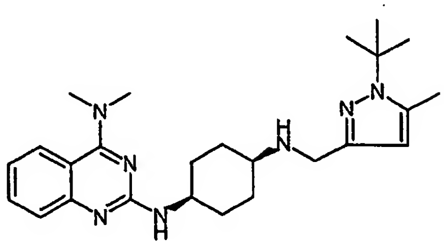
Example No.	Structure	APCI-MS
1182		408 (M + H)
1183		392 (M + H)
1184		476 (M + H)
1185		426 (M + H)
1186		496 (M + H)

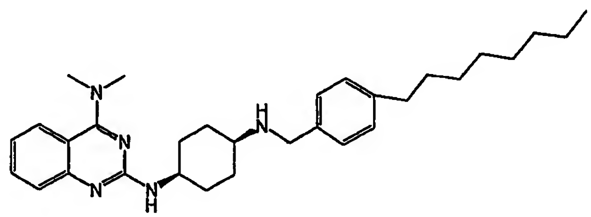
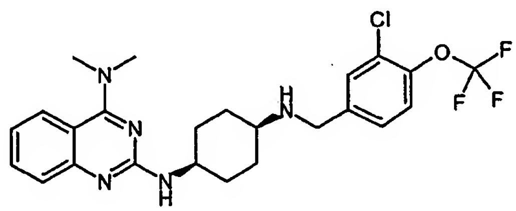
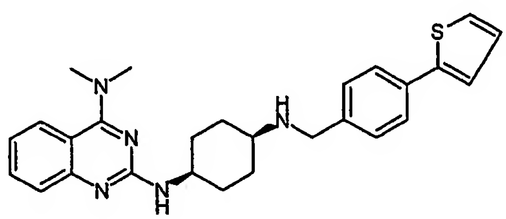
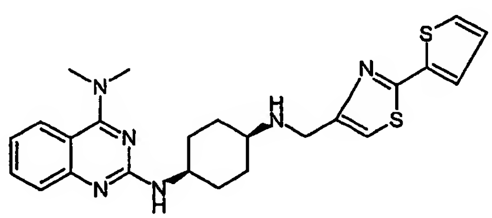
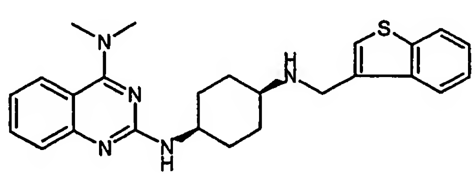
Example No.	Structure	APCI-MS
1187		442 (M + H)
1188		442 (M + H)
1189		408 (M + H)
1190		446 (M + H)
1191		458 (M + H)

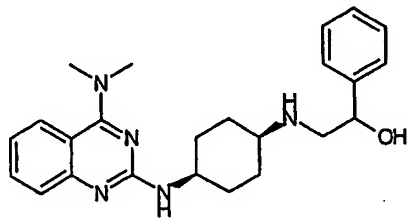
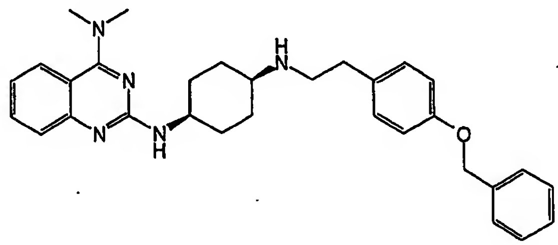
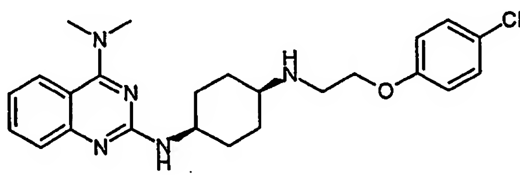
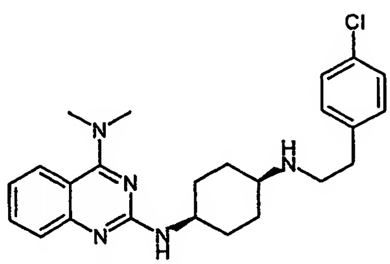
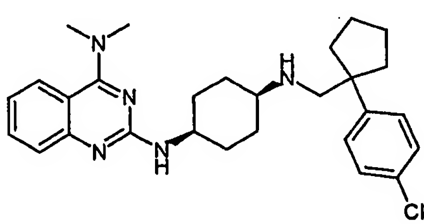
Example No.	Structure	APCI-MS
1192		484 (M + H)
1193		450 (M + H)
1194		404 (M + H)
1195		525 (M + H)
1196		483 (M + H)

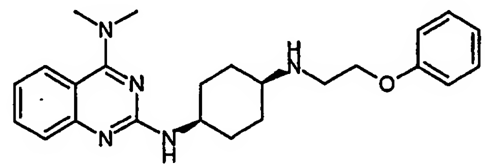
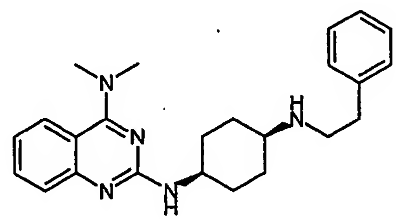
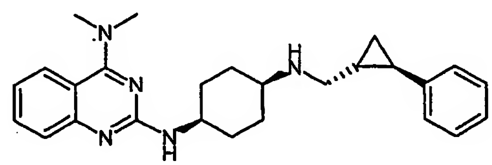
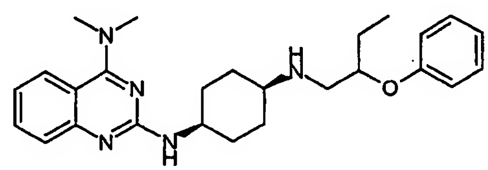
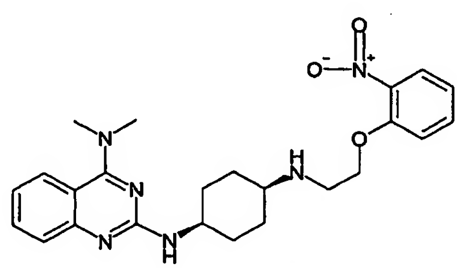
Example No.	Structure	APCI-MS
1197		544 (M + H)
1198		512 (M + H)
1199		436 (M + H)
1200		381 (M + H)
1201		539 (M + H)

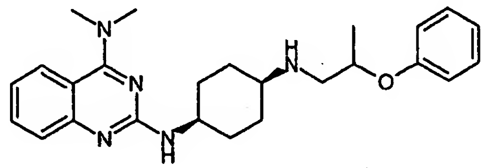
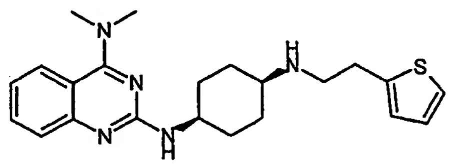
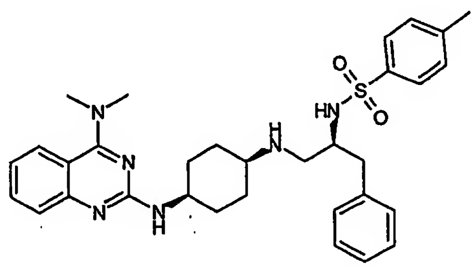
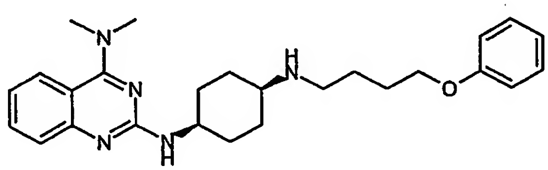
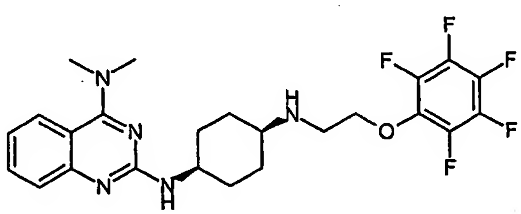
Example No.	Structure	APCI-MS
1202		486 (M + H)
1203		518 (M + H)
1204		436 (M + H)
1205		515 (M + H)
1206		501 (M + H)

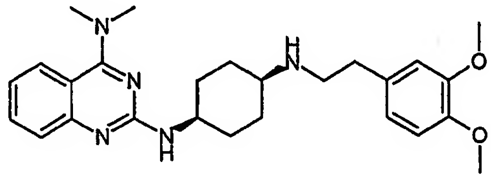
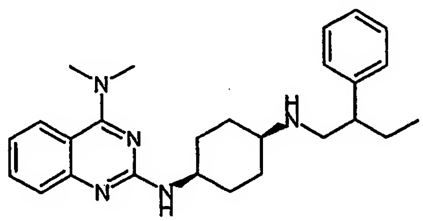
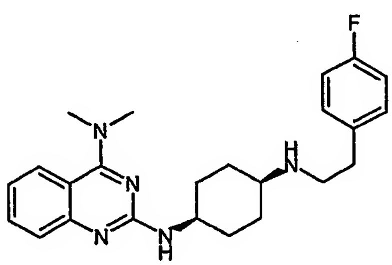
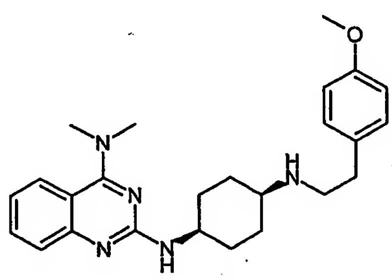
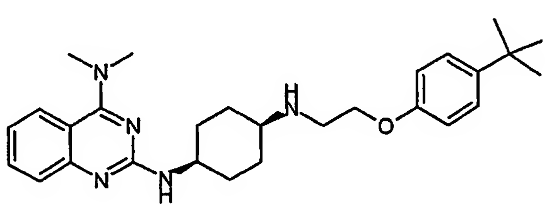
Example No.	Structure	APCI-MS
1207		580 (M + H)
1208		539 (M + H)
1209		459 (M + H)
1210		414 (M + H)
1211		436 (M + H)

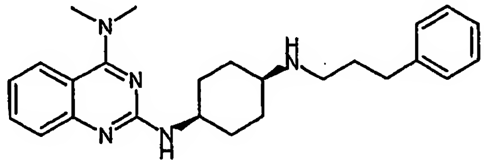
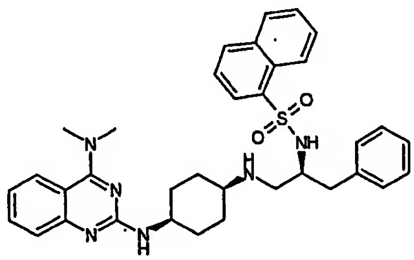
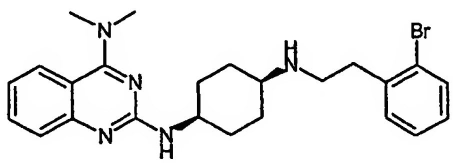
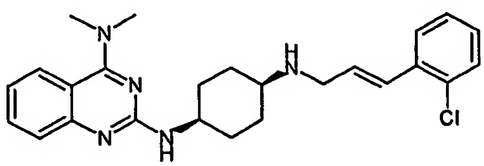
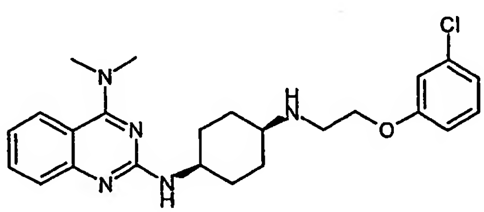
Example No.	Structure	APCI-MS
1212		488 (M + H)
1213		494 (M + H)
1214		458 (M + H)
1215		465 (M + H)
1216		432 (M + H)

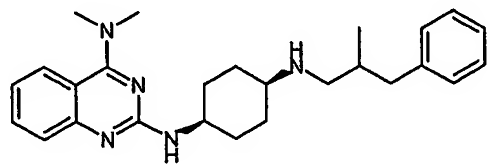
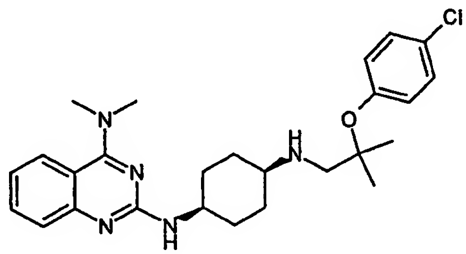
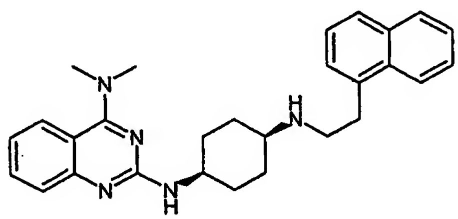
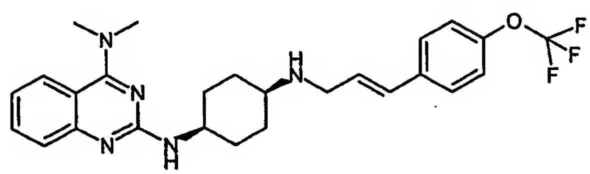
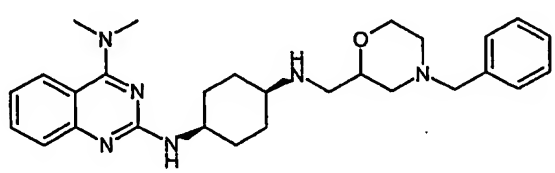
Example No.	Structure	APCI-MS
1217		406 (M + H)
1218		496 (M + H)
1219		440 (M + H)
1220		424 (M + H)
1221		478 (M + H)

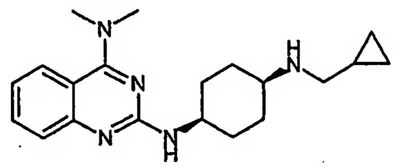
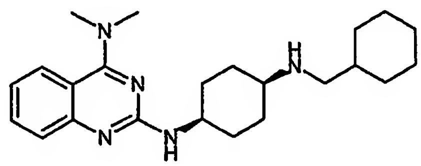
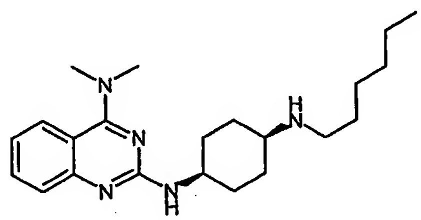
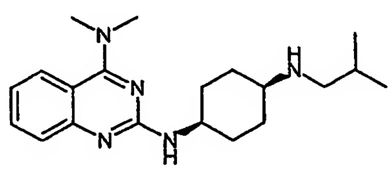
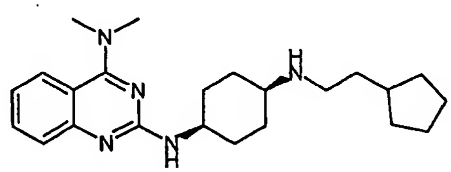
Example No.	Structure	APCI-MS
1222		406 (M + H)
1223		390 (M + H)
1224		416 (M + H)
1225		434 (M + H)
1226		451 (M + H)

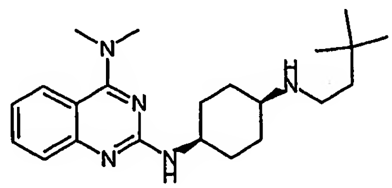
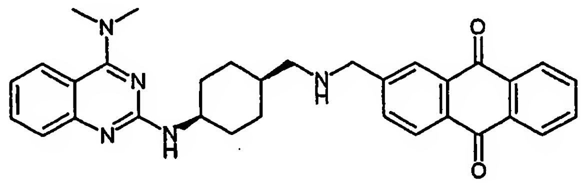
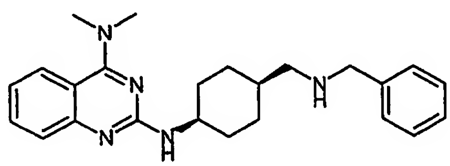
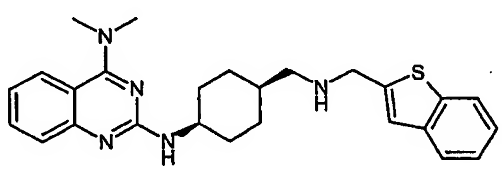
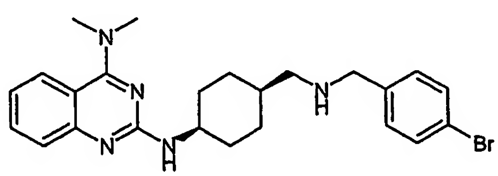
Example No.	Structure	APCI-MS
1227		420 (M + H)
1228		396 (M + H)
1229		573 (M + H)
1230		434 (M + H)
1231		496 (M + H)

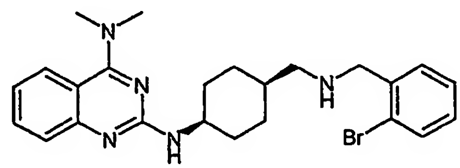
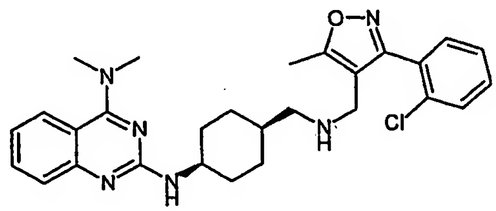
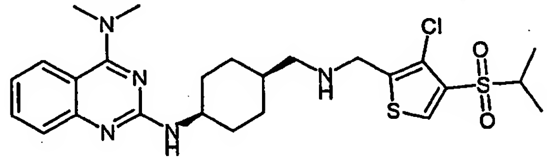
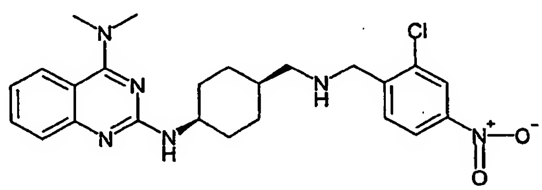
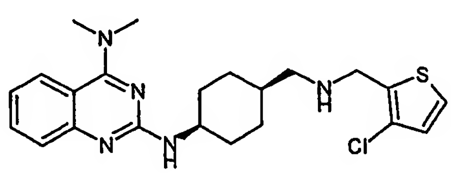
Example No.	Structure	APCI-MS
1232		450 (M + H)
1233		418 (M + H)
1234		408 (M + H)
1235		420 (M + H)
1236		462 (M + H)

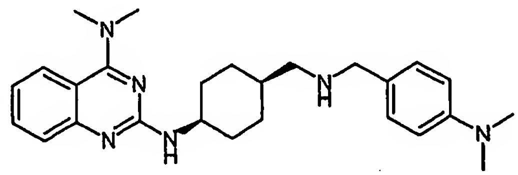
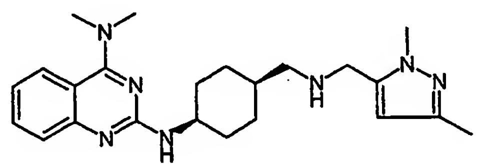
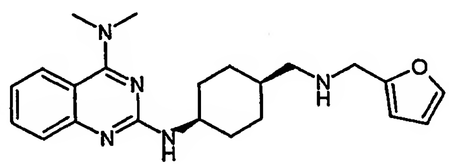
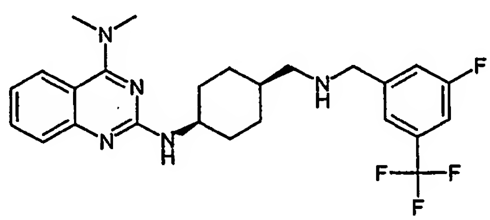
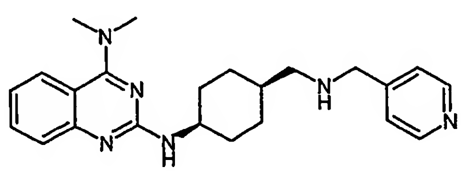
Example No.	Structure	APCI-MS
1237		404 (M + H)
1238		609 (M + H)
1239		468 (M + H)
1240		436 (M + H)
1241		440 (M + H)

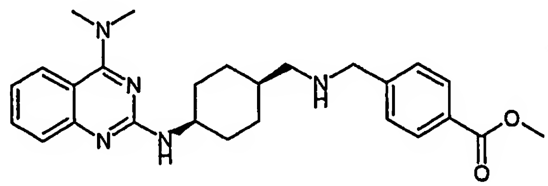
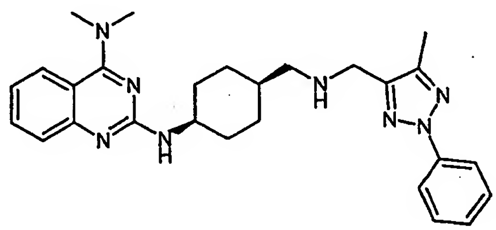
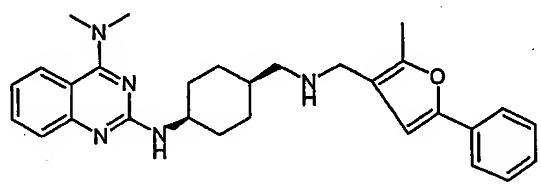
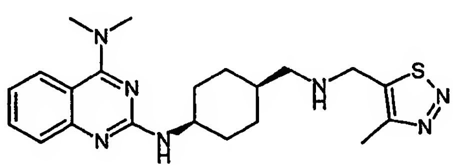
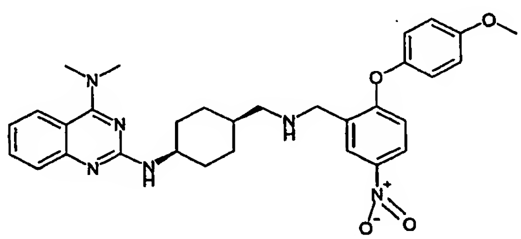
Example No.	Structure	APCI-MS
1242		418 (M + H)
1243		468 (M + H)
1244		440 (M + H)
1245		486 (M + H)
1246		475 (M + H)

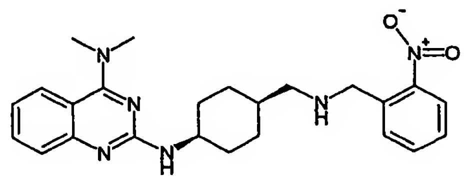
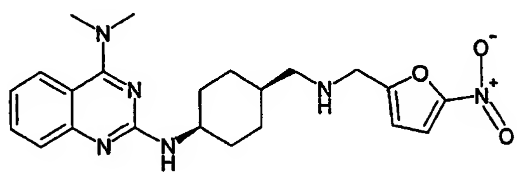
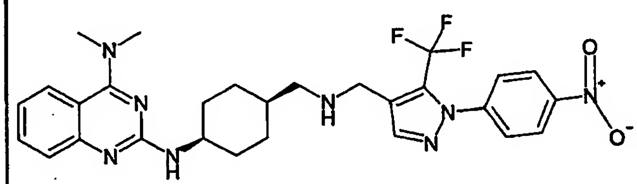
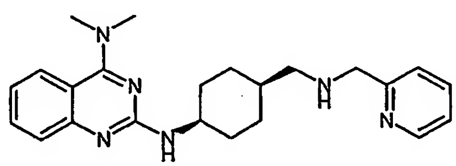
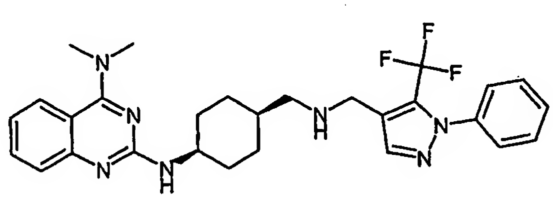
Example No.	Structure	APCI-MS
1247		340 (M + H)
1248		382 (M + H)
1249		370 (M + H)
1250		342 (M + H)
1251		382 (M + H)

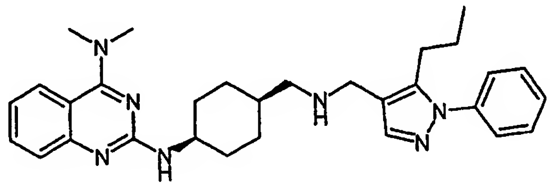
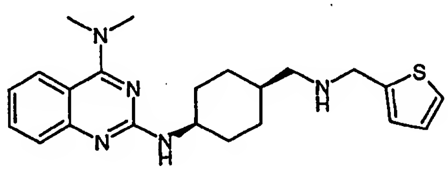
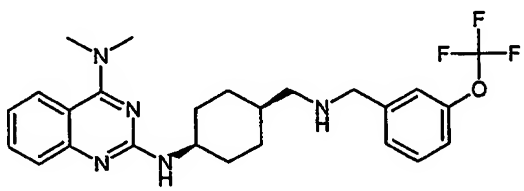
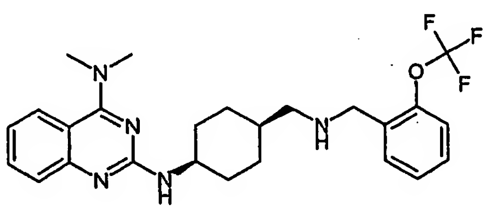
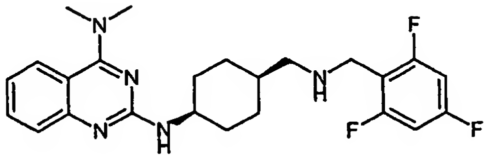
Example No.	Structure	APCI-MS
1252		370 (M + H)
1253		520 (M + H)
1254		390 (M + H)
1255		446 (M + H)
1256		468 (M + H)

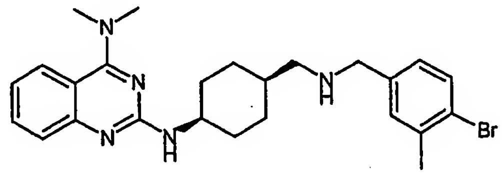
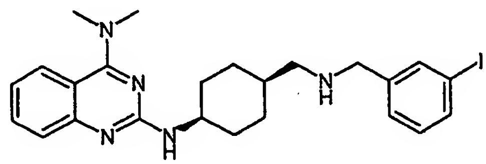
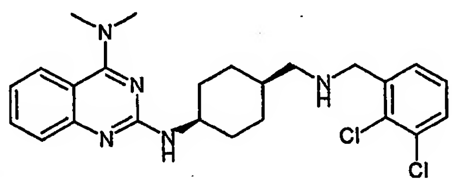
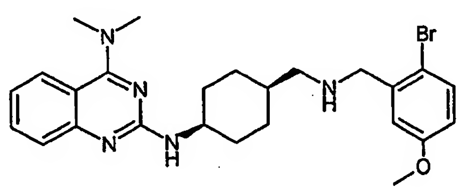
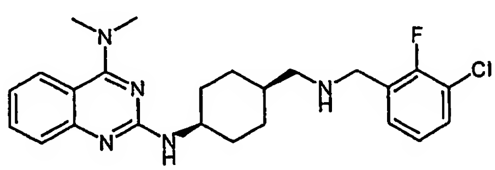
Example No.	Structure	APCI-MS
1257		468 (M + H)
1258		505 (M + H)
1259		536 (M + H)
1260		469 (M + H)
1261		430 (M + H)

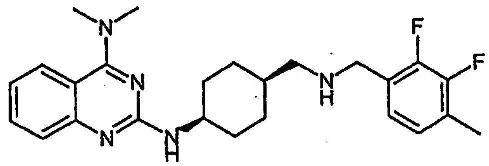
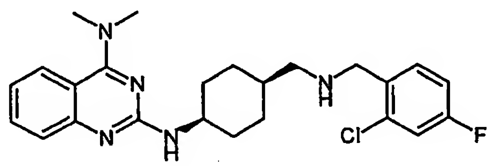
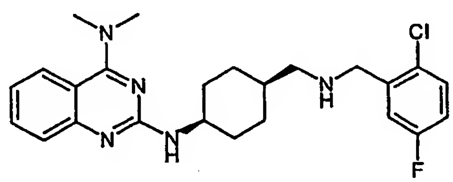
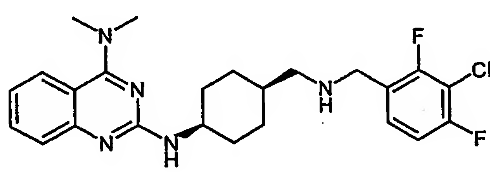
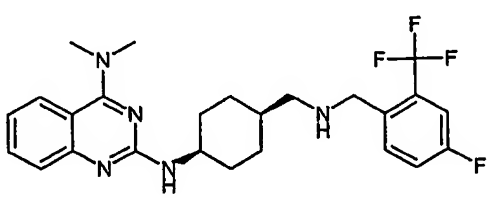
Example No.	Structure	APCI-MS
1262		433 (M + H)
1263		408 (M + H)
1264		380 (M + H)
1265		476 (M + H)
1266		391 (M + H)

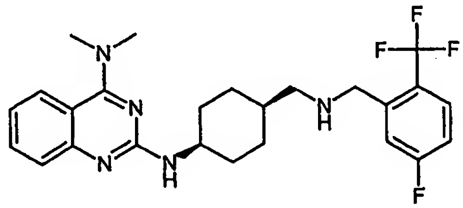
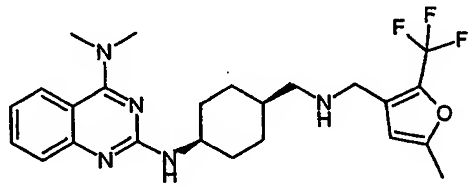
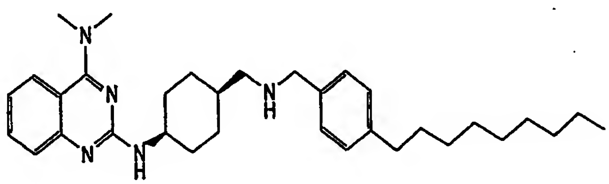
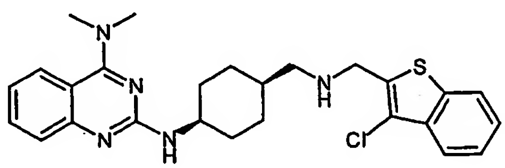
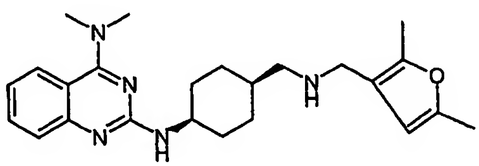
Example No.	Structure	APCI-MS
1267		448 (M + H)
1268		471 (M + H)
1269		470 (M + H)
1270		412 (M + H)
1271		557 (M + H)

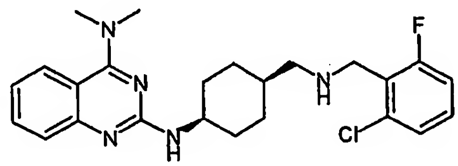
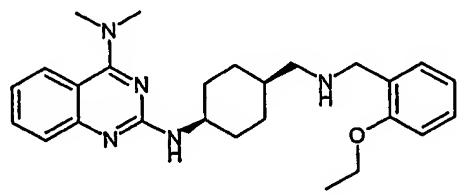
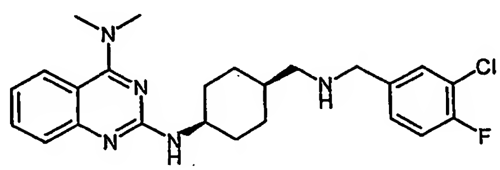
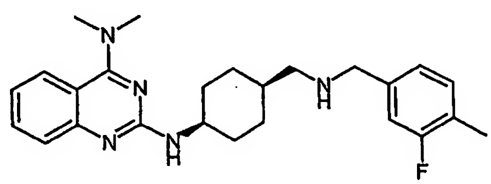
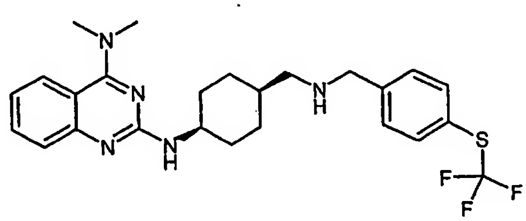
Example No.	Structure	APCI-MS
1272		435 (M + H)
1273		425 (M + H)
1274		569 (M + H)
1275		391 (M + H)
1276		524 (M + H)

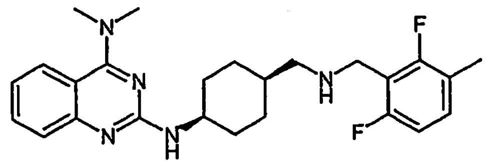
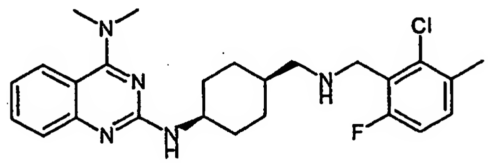
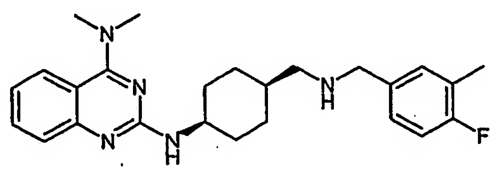
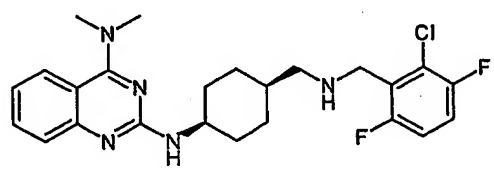
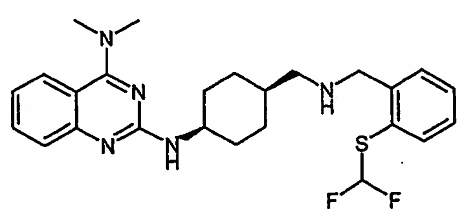
Example No.	Structure	APCI-MS
1277		498 (M + H)
1278		396 (M + H)
1279		474 (M + H)
1280		474 (M + H)
1281		444 (M + H)

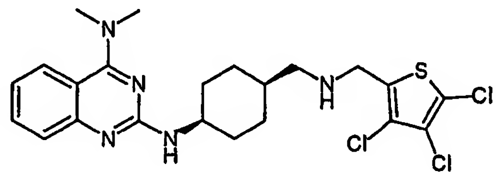
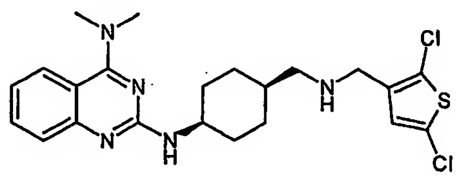
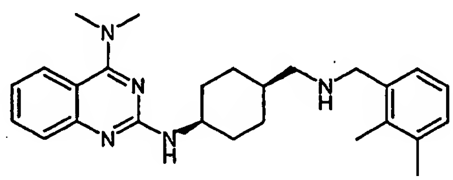
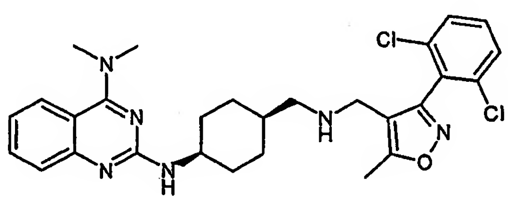
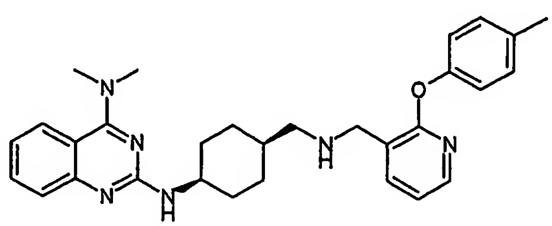
Example No.	Structure	APCI-MS
1282		482 (M + H)
1283		516 (M + H)
1284		458 (M + H)
1285		498 (M + H)
1286		442 (M + H)

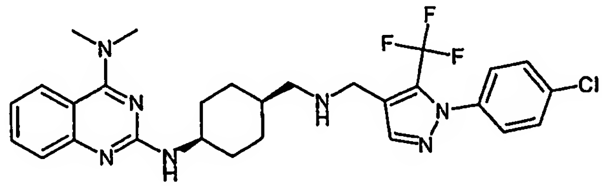
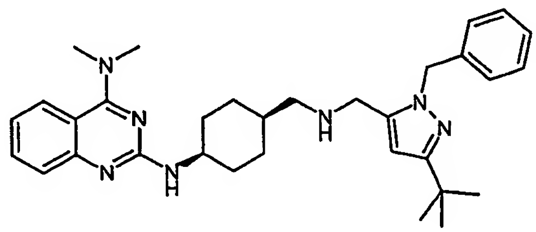
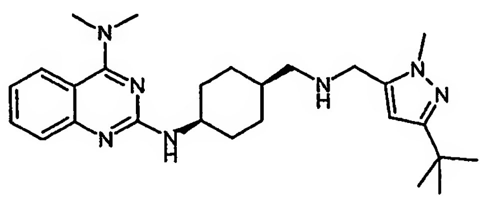
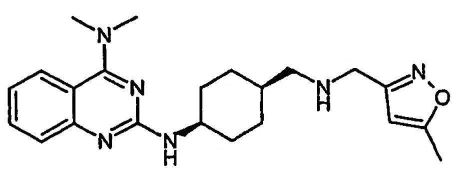
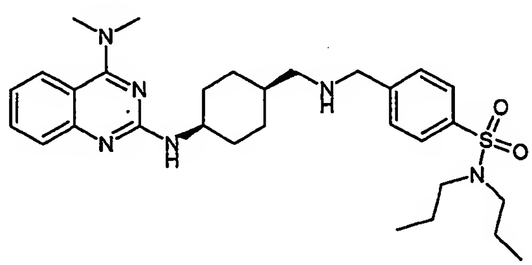
Example No.	Structure	APCI-MS
1287		440 (M + H)
1288		442 (M + H)
1289		442 (M + H)
1290		460 (M + H)
1291		476 (M + H)

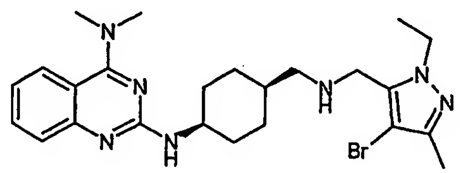
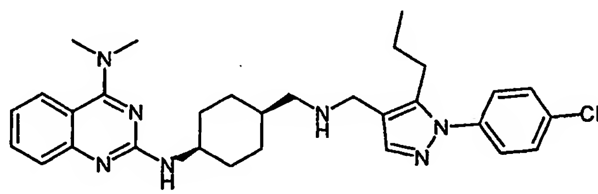
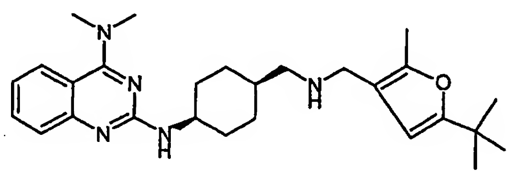
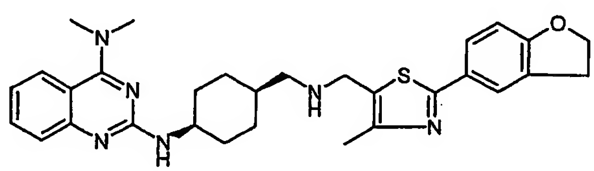
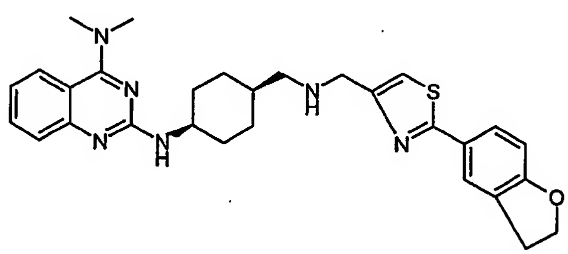
Example No.	Structure	APCI-MS
1292		476 (M + H)
1293		462 (M + H)
1294		516 (M + H)
1295		480 (M + H)
1296		408 (M + H)

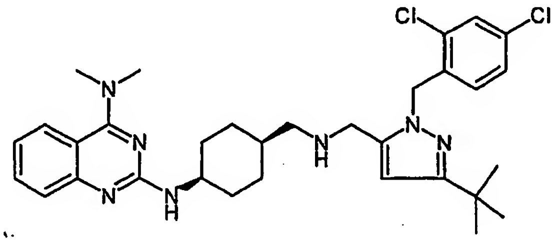
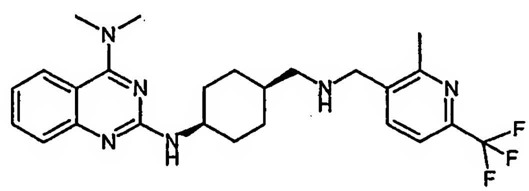
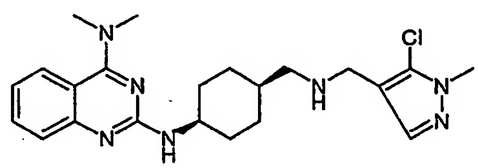
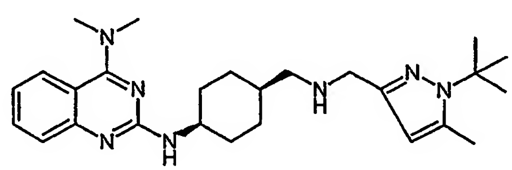
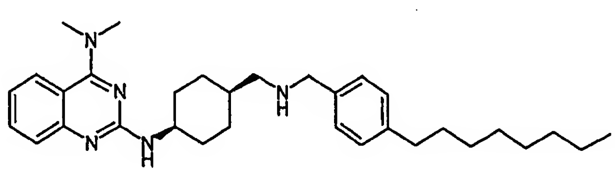
Example No.	Structure	APCI-MS
1297		442 (M + H)
1298		434 (M + H)
1299		442 (M + H)
1300		422 (M + H)
1301		490 (M + H)

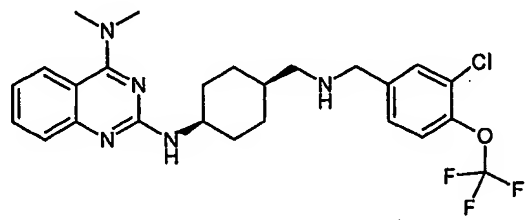
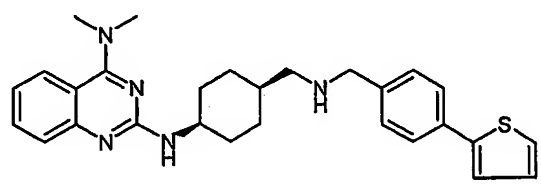
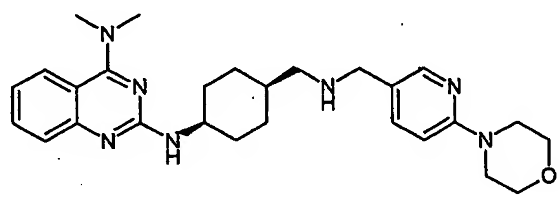
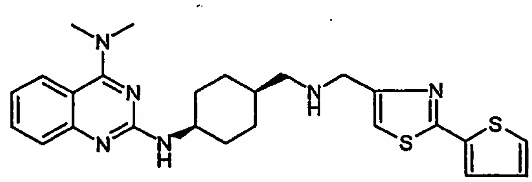
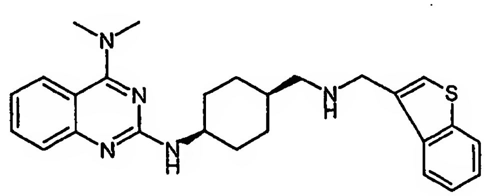
Example No.	Structure	APCI-MS
1302		440 (M + H)
1303		456 (M + H)
1304		422 (M + H)
1305		460 (M + H)
1306		472 (M + H)

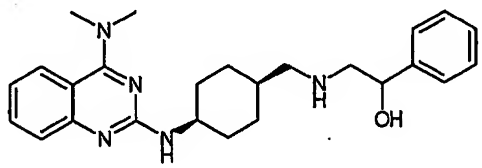
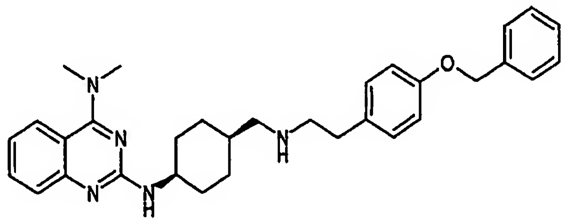
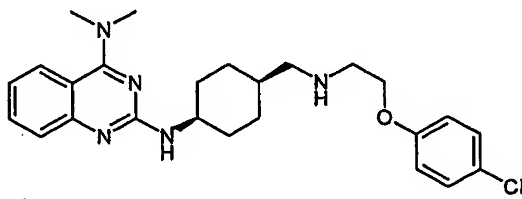
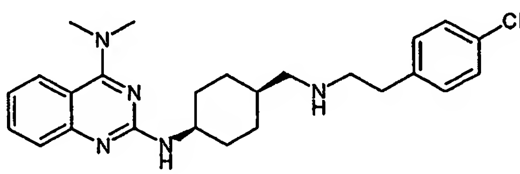
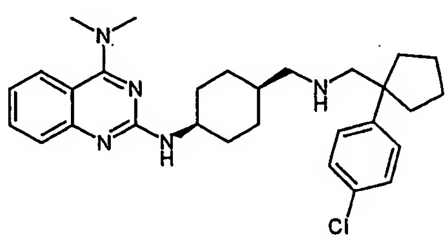
Example No.	Structure	APCI-MS
1307		498 (M + H)
1308		464 (M + H)
1309		418 (M + H)
1310		539 (M + H)
1311		497 (M + H)

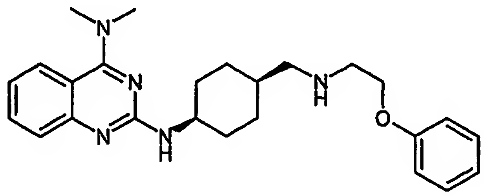
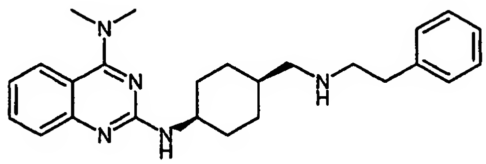
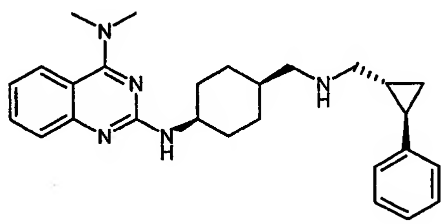
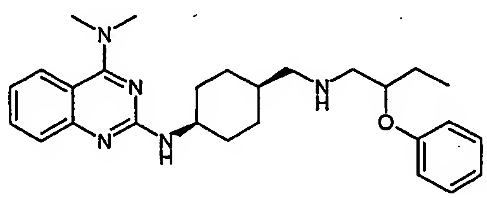
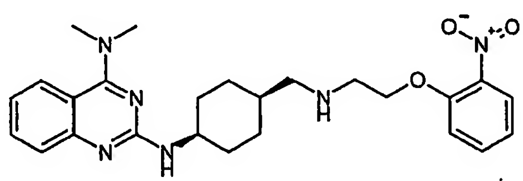
Example No.	Structure	APCI-MS
1312		558 (M + H)
1313		526 (M + H)
1314		450 (M + H)
1315		395 (M + H)
1316		553 (M + H)

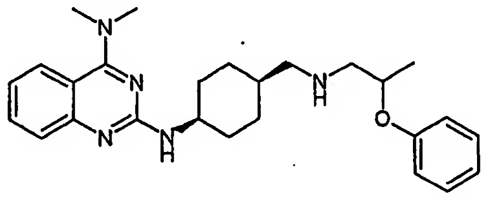
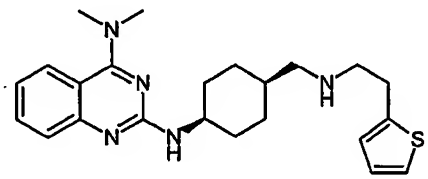
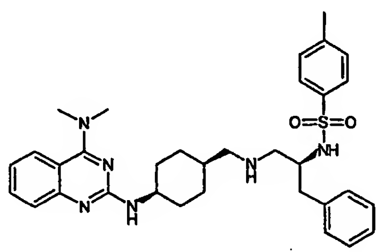
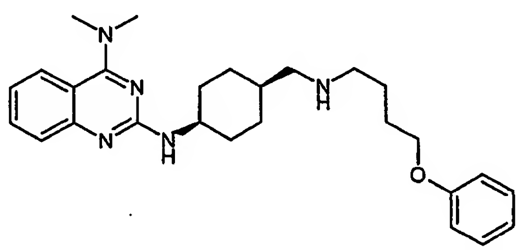
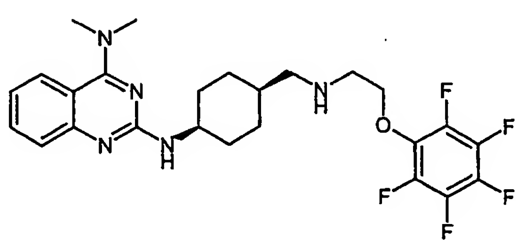
Example No.	Structure	APCI-MS
1317		500 (M + H)
1318		532 (M + H)
1319		450 (M + H)
1320		529 (M + H)
1321		515 (M + H)

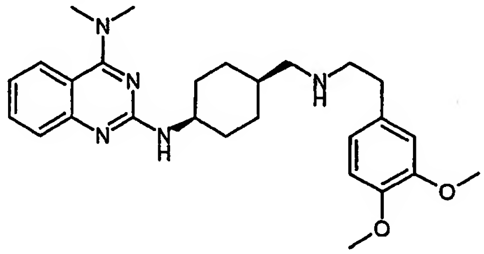
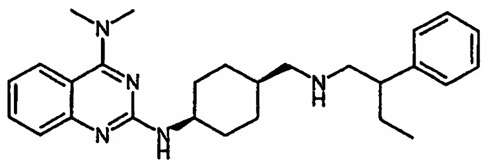
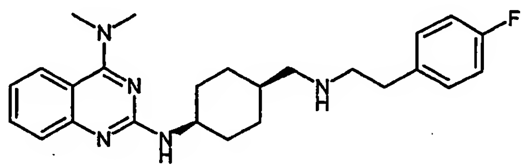
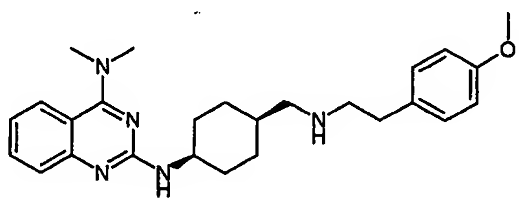
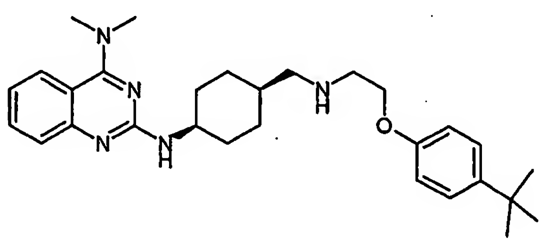
Example No.	Structure	APCI-MS
1322		594 (M + H)
1323		473 (M + H)
1324		428 (M + H)
1325		450 (M + H)
1326		502 (M + H)

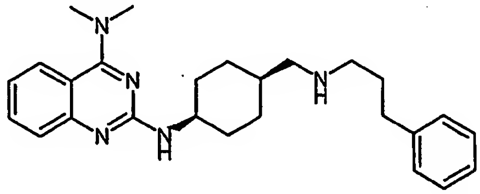
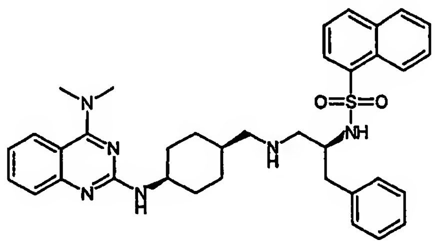
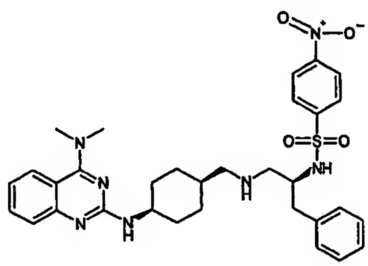
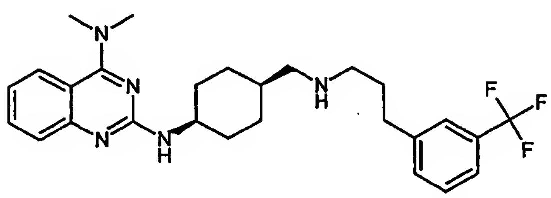
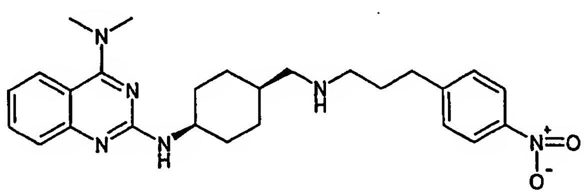
Example No.	Structure	APCI-MS
1327		508 (M + H)
1328		472 (M + H)
1329		476 (M + H)
1330		479 (M + H)
1331		446 (M + H)

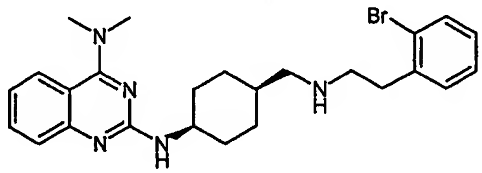
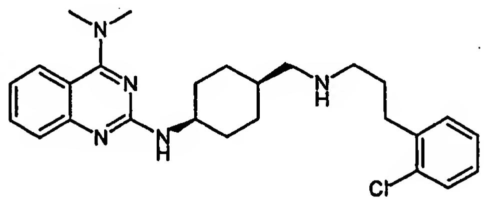
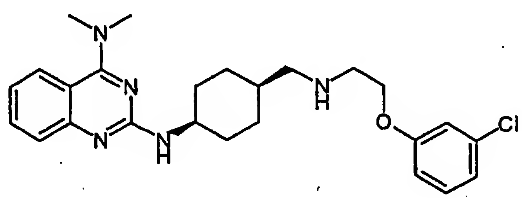
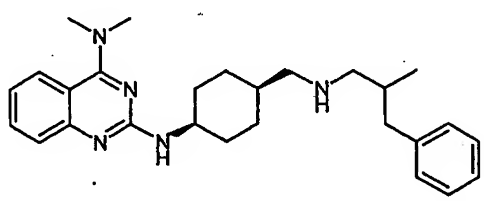
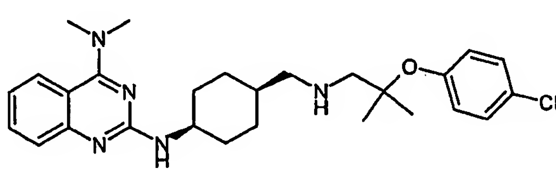
Example No.	Structure	APCI-MS
1332		420 (M + H)
1333		510 (M + H)
1334		454 (M + H)
1335		438 (M + H)
1336		492 (M + H)

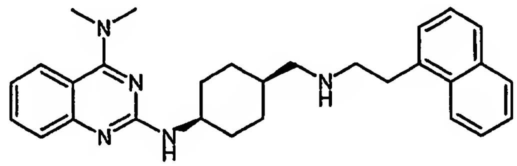
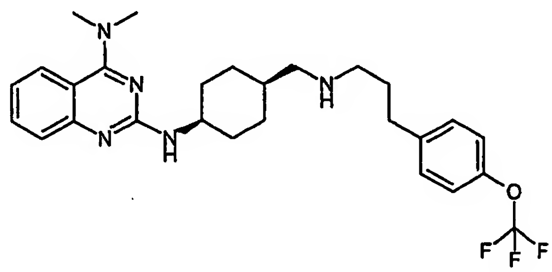
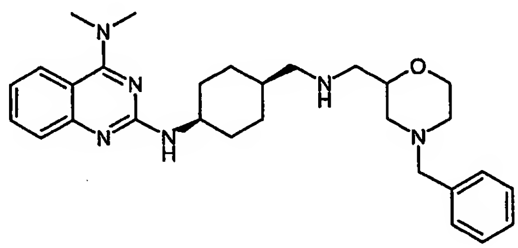
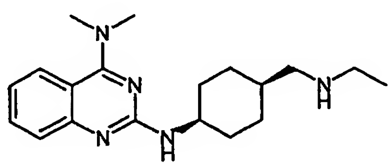
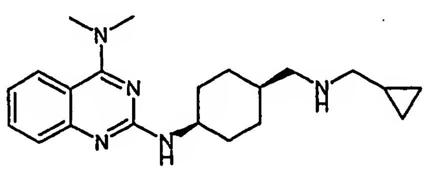
Example No.	Structure	APCI-MS
1337		420 (M + H)
1338		404 (M + H)
1339		430 (M + H)
1340		448 (M + H)
1341		465 (M + H)

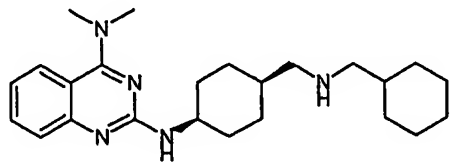
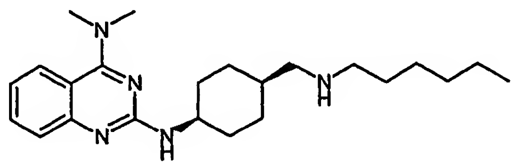
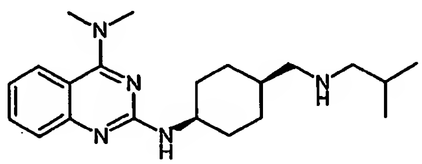
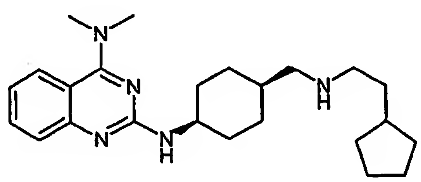
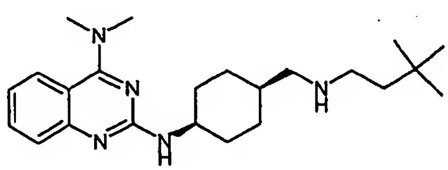
Example No.	Structure	APCI-MS
1342		434 (M + H)
1343		410 (M + H)
1344		587 (M + H)
1345		448 (M + H)
1346		510 (M + H)

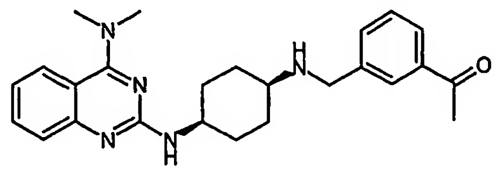
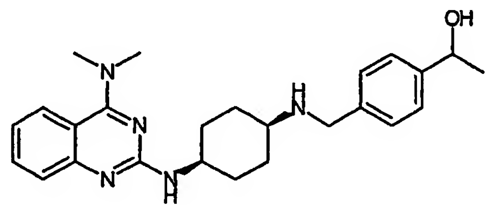
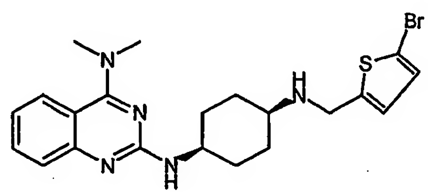
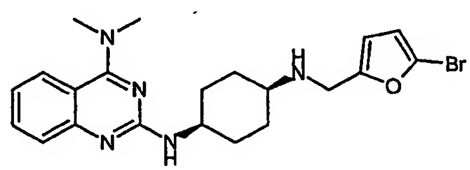
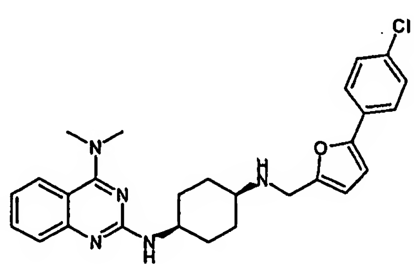
Example No.	Structure	APCI-MS
1347		464 (M + H)
1348		432 (M + H)
1349		422 (M + H)
1350		434 (M + H)
1351		476 (M + H)

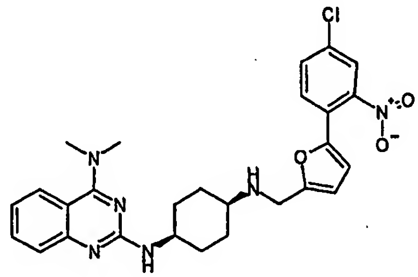
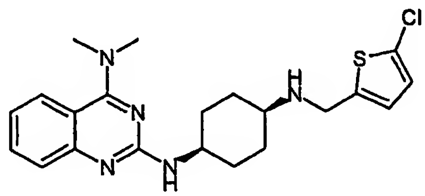
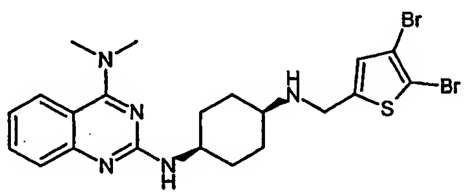
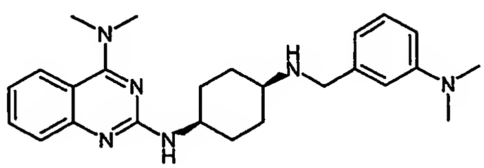
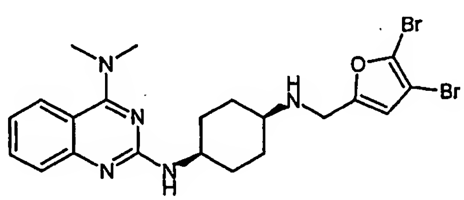
Example No.	Structure	APCI-MS
1352		418 (M + H)
1353		623 (M + H)
1354		618 (M + H)
1355		486 (M + H)
1356		463 (M + H)

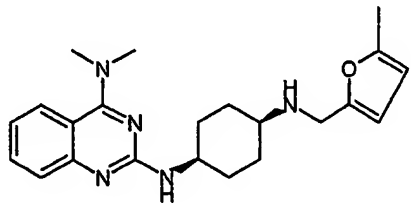
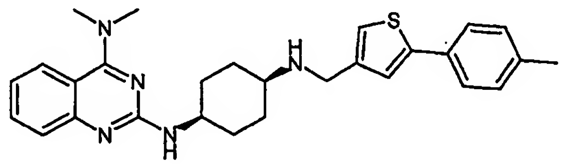
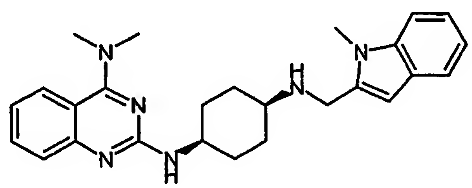
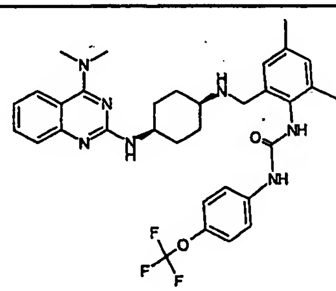
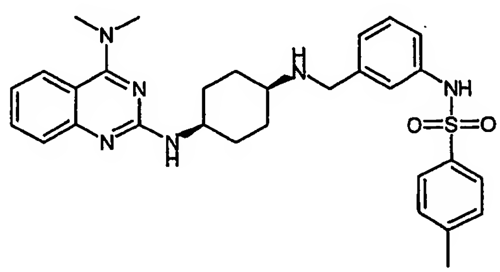
Example No.	Structure	APCI-MS
1357		482 (M + H)
1358		452 (M + H)
1359		454 (M + H)
1360		432 (M + H)
1361		482 (M + H)

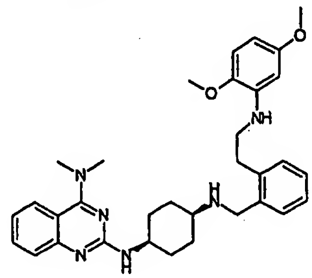
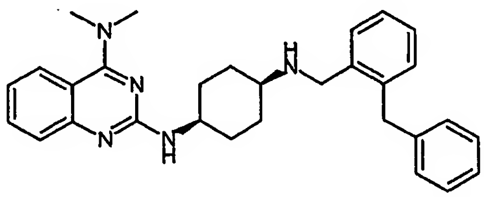
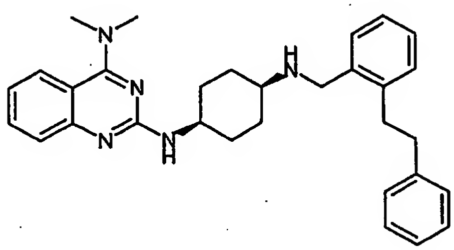
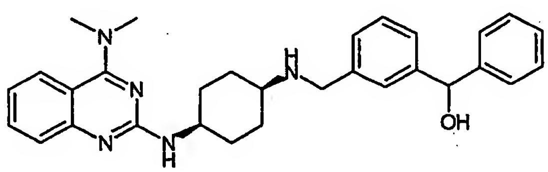
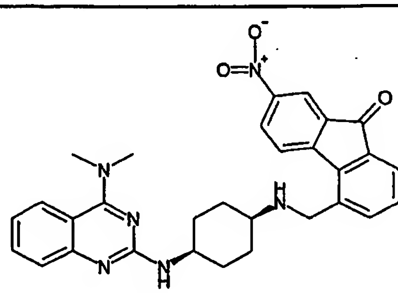
Example No.	Structure	APCI-MS
1362		454 (M + H)
1363		502 (M + H)
1364		489 (M + H)
1365		328 (M + H)
1366		354 (M + H)

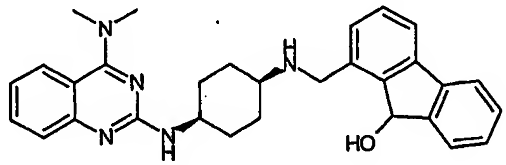
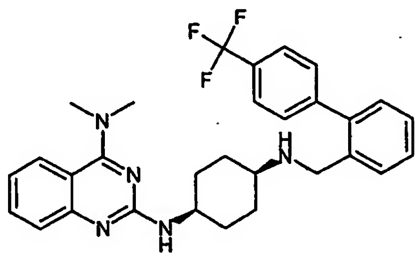
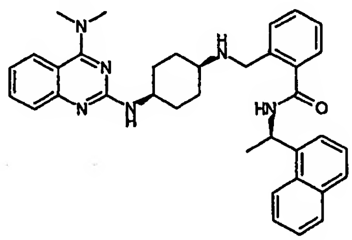
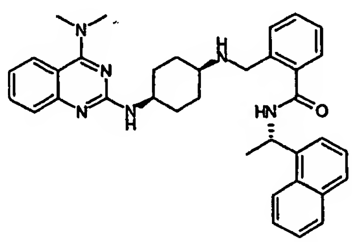
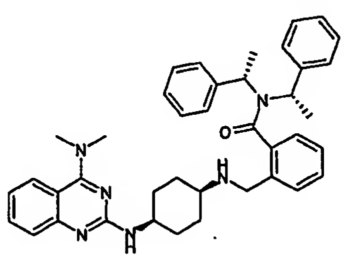
Example No.	Structure	APCI-MS
1367		396 (M + H)
1368		384 (M + H)
1369		356 (M + H)
1370		396 (M + H)
1371		384 (M + H)

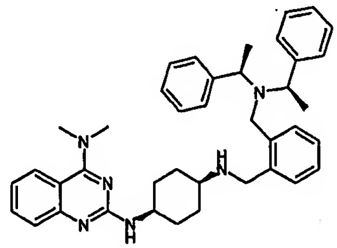
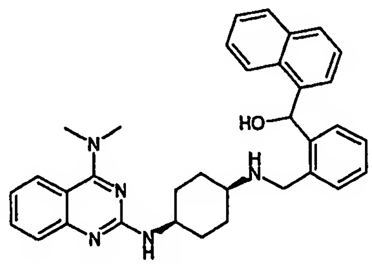
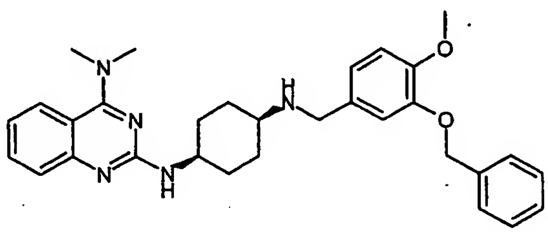
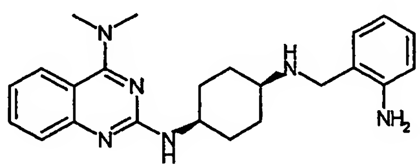
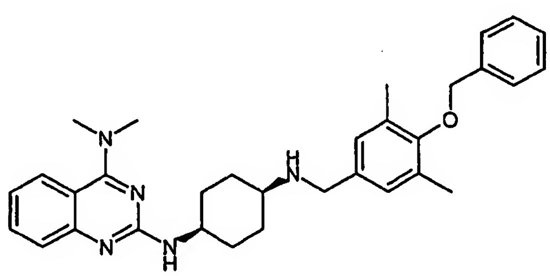
Example No.	Structure	APCI-MS
1372		418 (M + H)
1373		420 (M + H)
1374		460 (M + H)
1375		444 (M + H)
1376		476 (M + H)

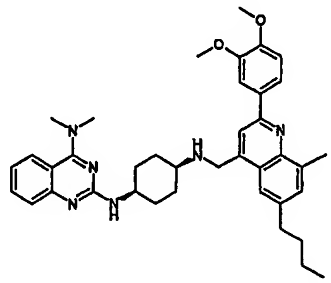
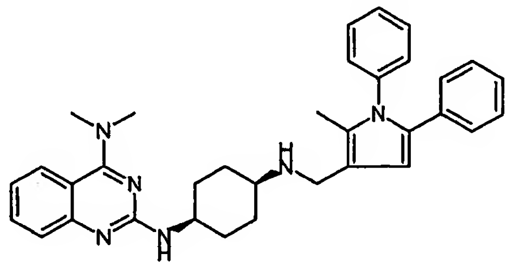
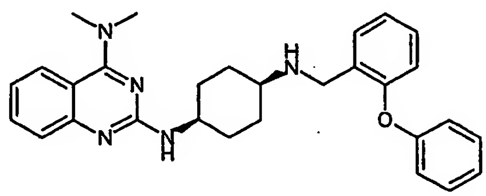
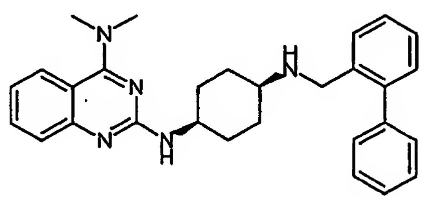
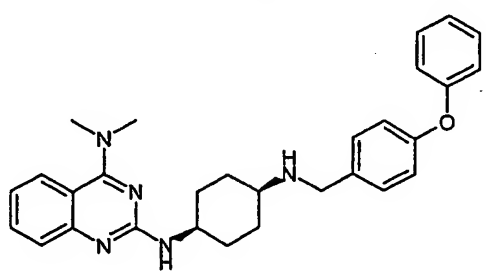
Example No.	Structure	APCI-MS
1377		521 (M + H)
1378		416 (M + H)
1379		538 (M + H)
1380		419 (M + H)
1381		522 (M + H)

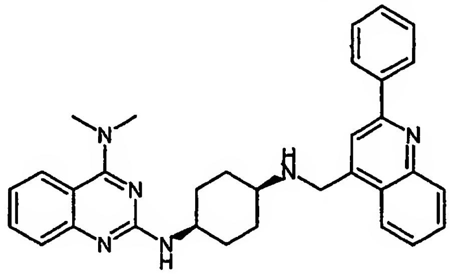
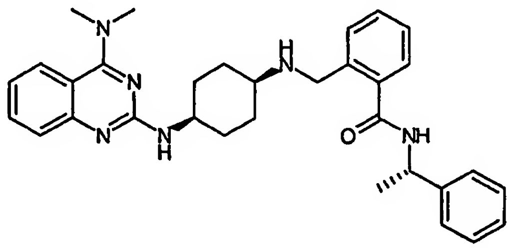
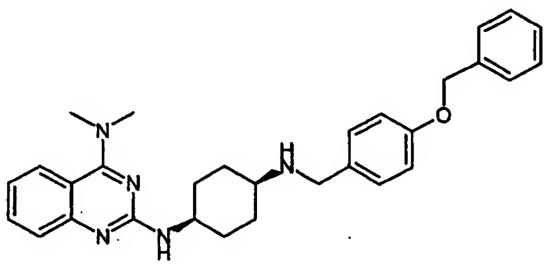
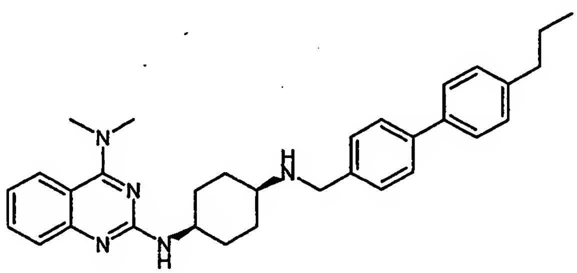
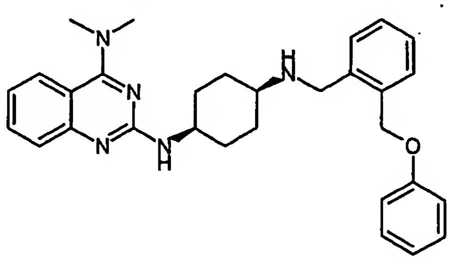
Example No.	Structure	APCI-MS
1382		492 (M + H)
1383		472 (M + H)
1384		429 (M + H)
1385		622 (M + H)
1386		545 (M + H)

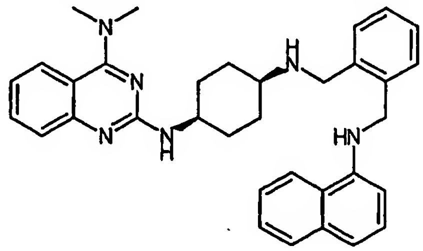
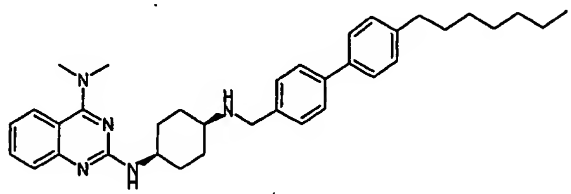
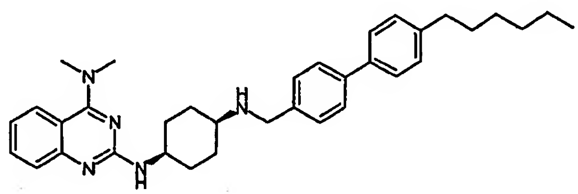
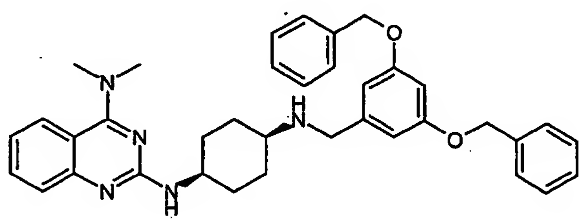
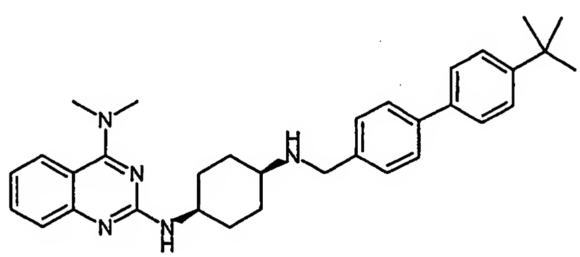
Example No.	Structure	APCI-MS
1387		555 (M + H)
1388		466 (M + H)
1389		480 (M + H)
1390		482 (M + H)
1391		523 (M + H)

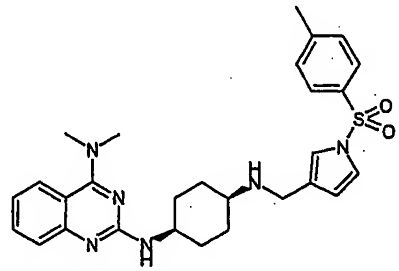
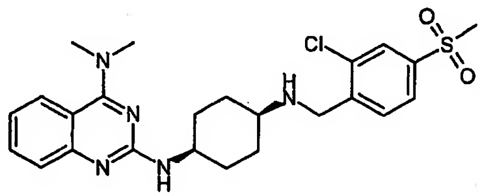
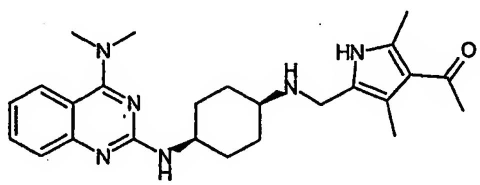
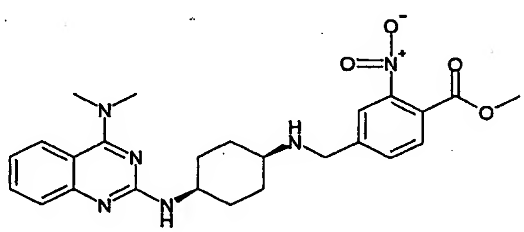
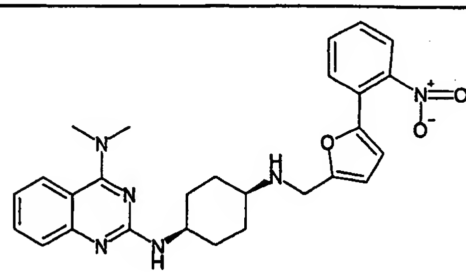
Example No.	Structure	APCI-MS
1392		480 (M + H)
1393		520 (M + H)
1394		573 (M + H)
1395		573 (M + H)
1396		627 (M + H)

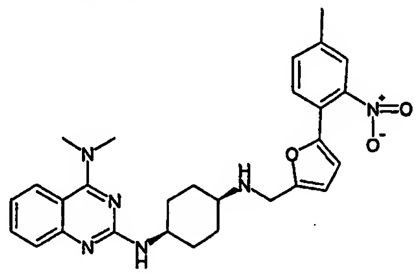
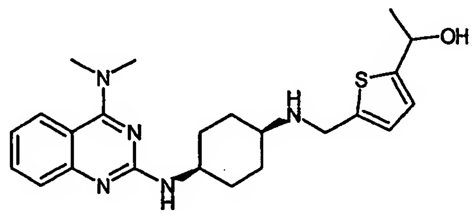
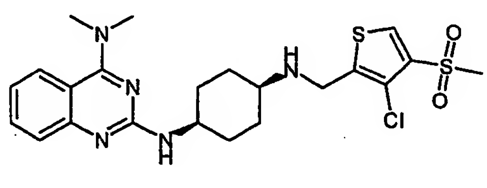
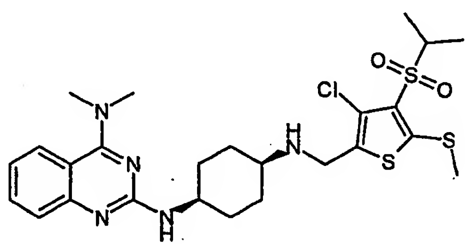
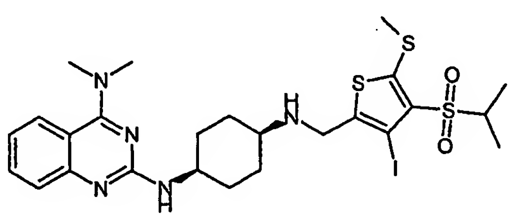
Example No.	Structure	APCI-MS
1397		613 (M + H)
1398		532 (M + H)
1399		512 (M + H)
1400		391 (M + H)
1401		510 (M + H)

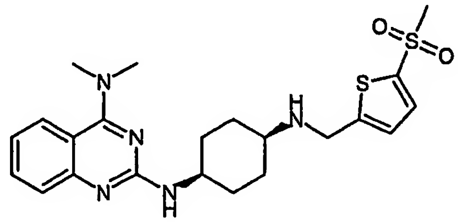
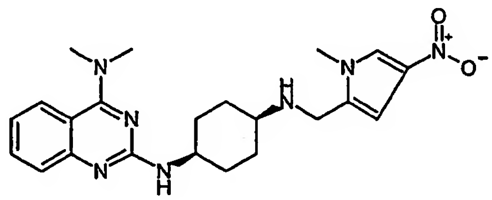
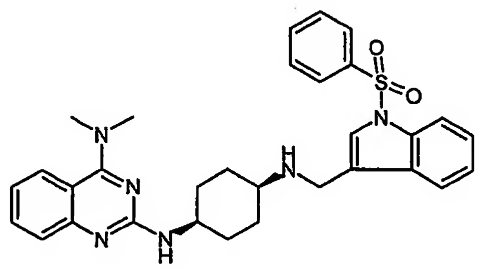
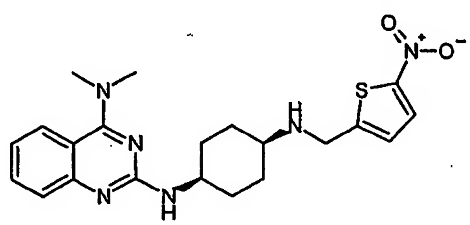
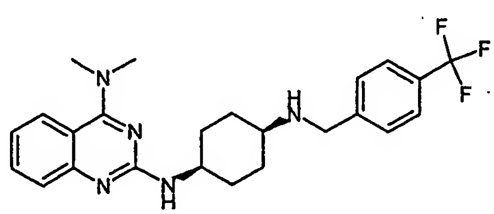
Example No.	Structure	APCI-MS
1402		633 (M + H)
1403		531 (M + H)
1404		468 (M + H)
1405		452 (M + H)
1406		468 (M + H)

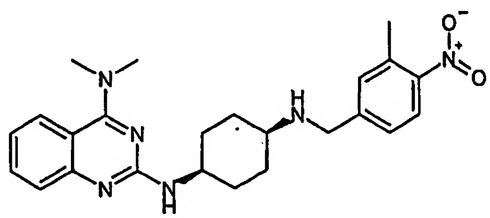
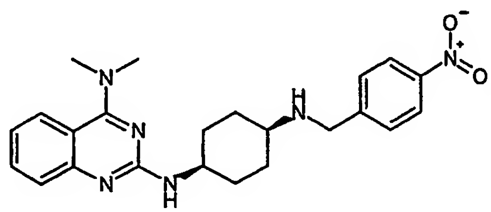
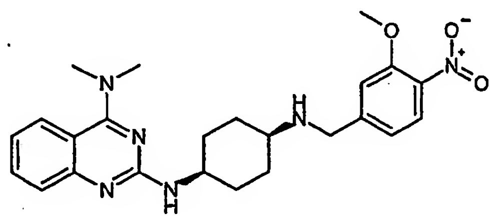
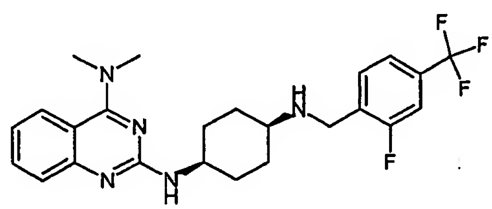
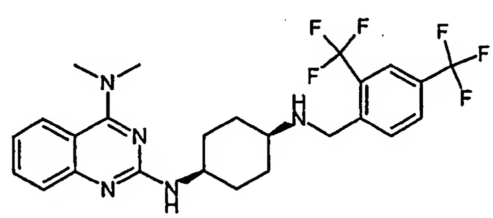
Example No.	Structure	APCI-MS
1407		503 (M + H)
1408		523 (M + H)
1409		482 (M + H)
1410		494 (M + H)
1411		482 (M + H)

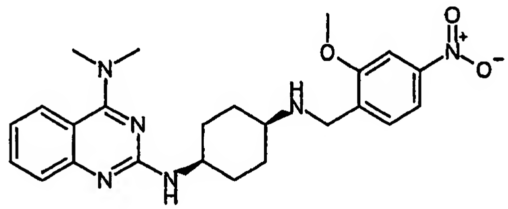
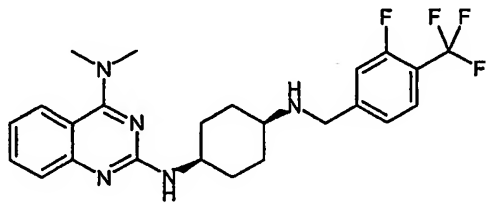
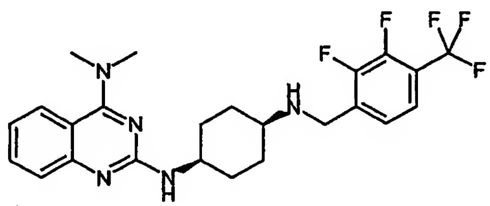
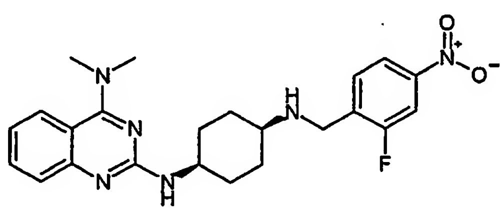
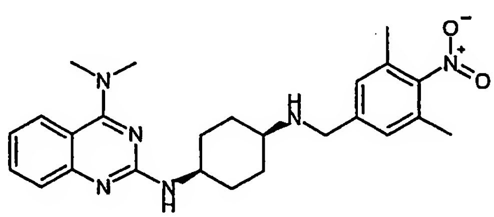
Example No.	Structure	APCI-MS
1412		531 (M + H)
1413		550 (M + H)
1414		536 (M + H)
1415		588 (M + H)
1416		508 (M + H)

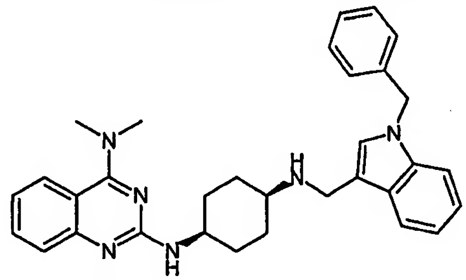
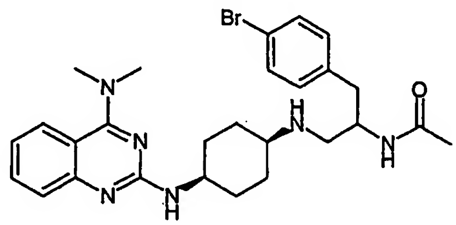
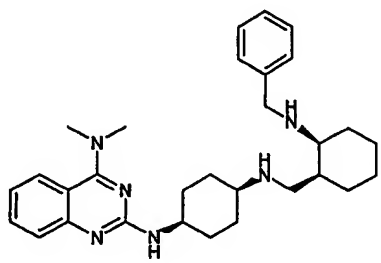
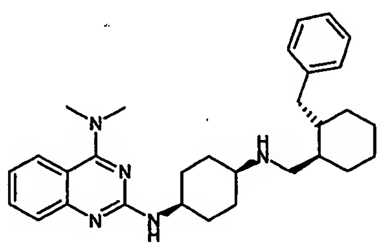
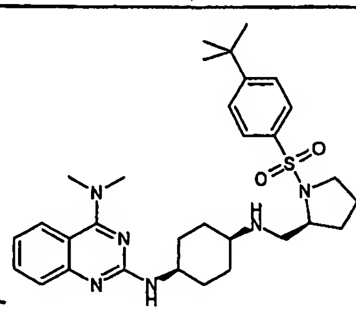
Example No.	Structure	APCI-MS
1417		519 (M + H)
1418		488 (M + H)
1419		435 (M + H)
1420		479 (M + H)
1421		487 (M + H)

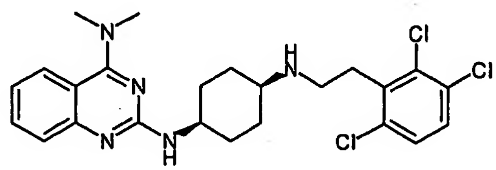
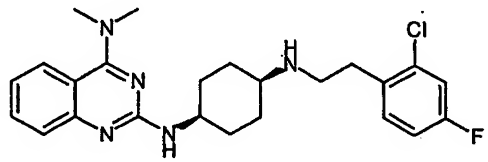
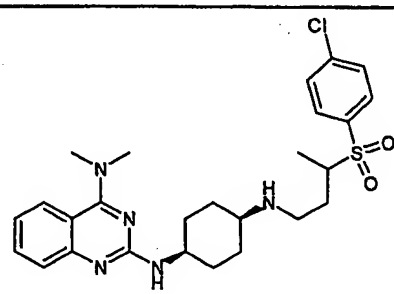
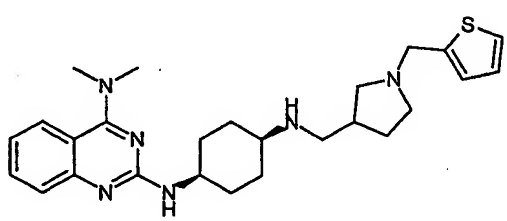
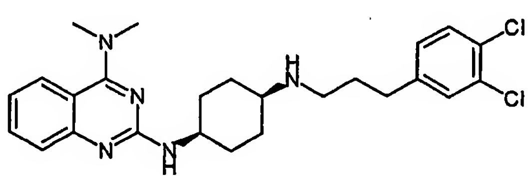
Example No.	Structure	APCI-MS
1422		501 (M + H)
1423		426 (M + H)
1424		494 (M + H)
1425		568 (M + H)
1426		660 (M + H)

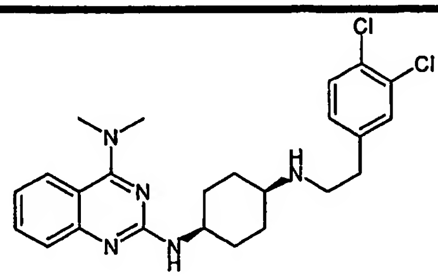
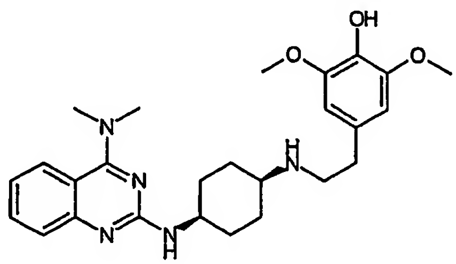
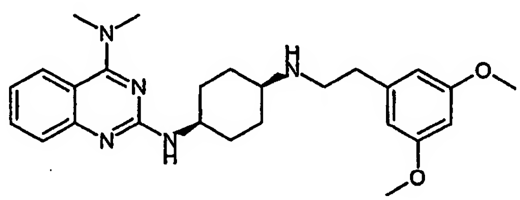
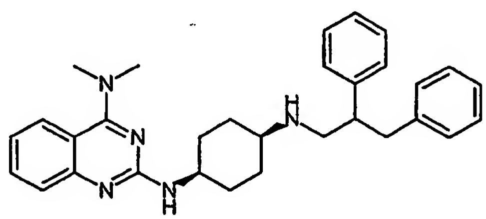
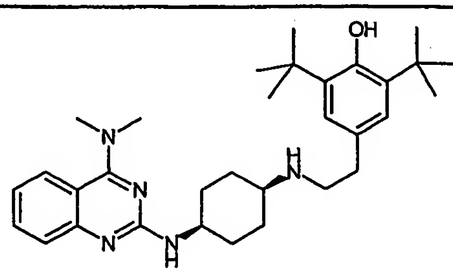
Example No.	Structure	APCI-MS
1427		460 (M + H)
1428		424 (M + H)
1429		555 (M + H)
1430		427 (M + H)
1431		444 (M + H)

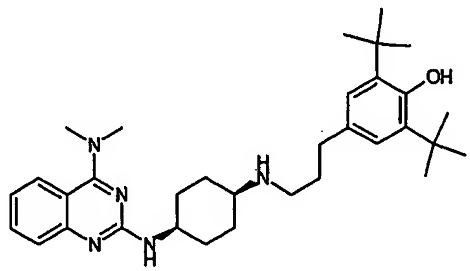
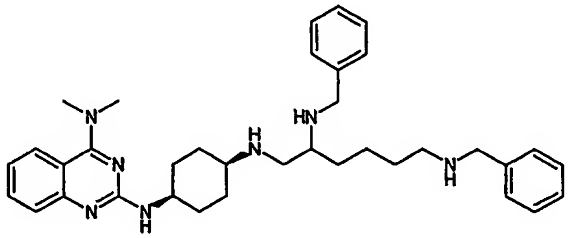
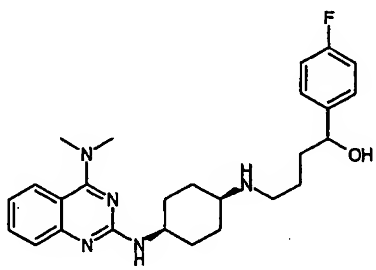
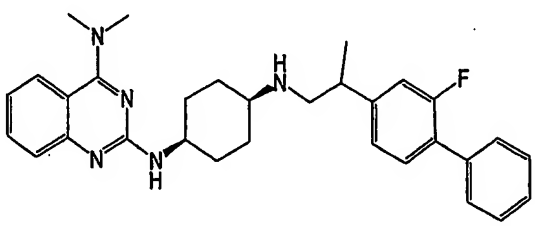
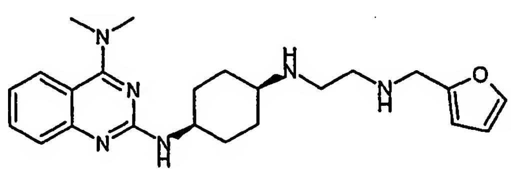
Example No.	Structure	APCI-MS
1432		435 (M+H)
1433		421 (M+H)
1434		451 (M+H)
1435		462 (M+H)
1436		512 (M+H)

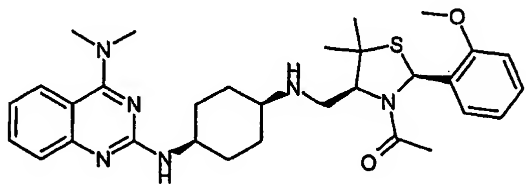
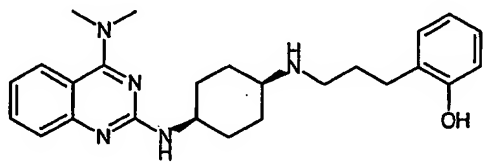
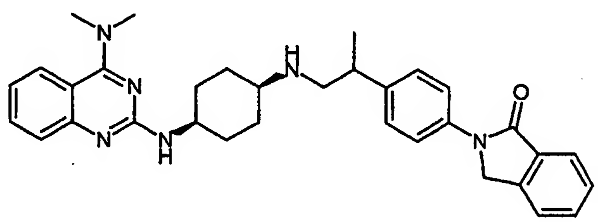
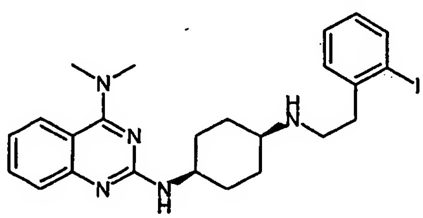
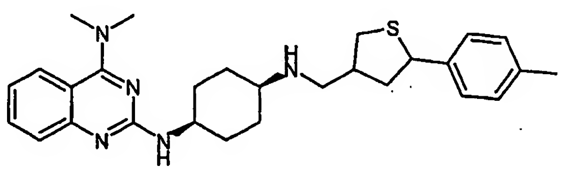
Example No.	Structure	APCI-MS
1437		451 (M + H)
1438		462 (M + H)
1439		480 (M + H)
1440		439 (M + H)
1441		449 (M + H)

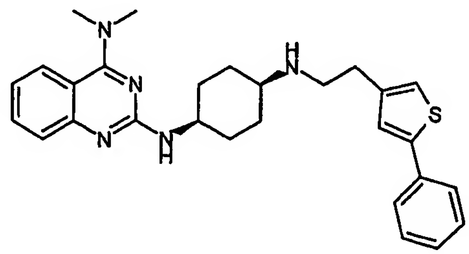
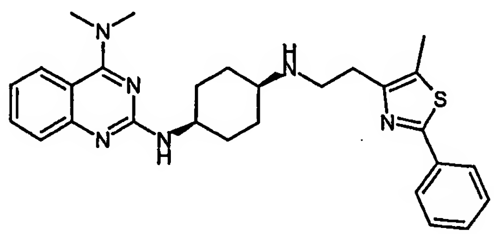
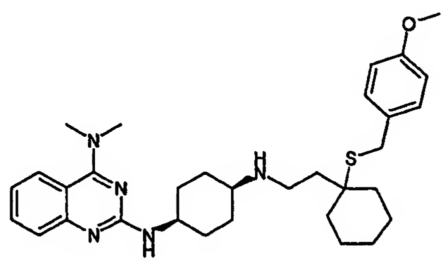
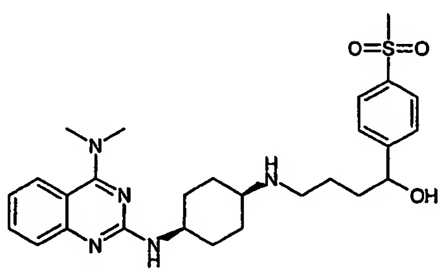
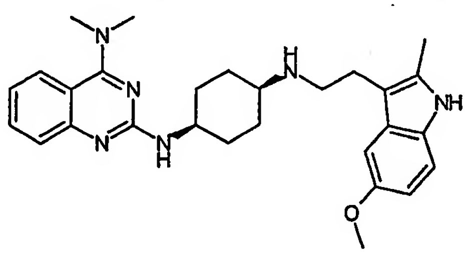
Example No.	Structure	APCI-MS
1442		505 (M + H)
1443		539 (M + H)
1444		487 (M + H)
1445		488 (M + H)
1446		565 (M + H)

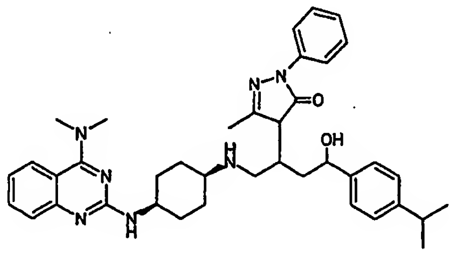
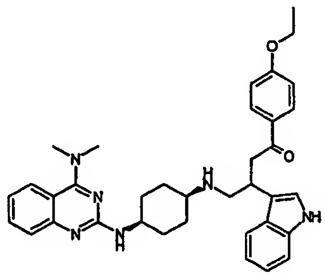
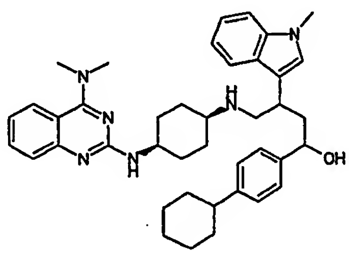
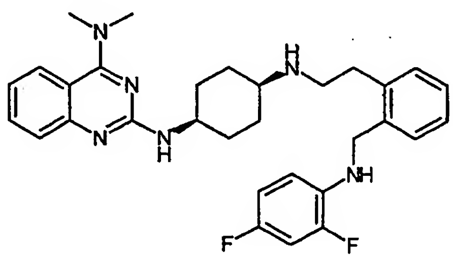
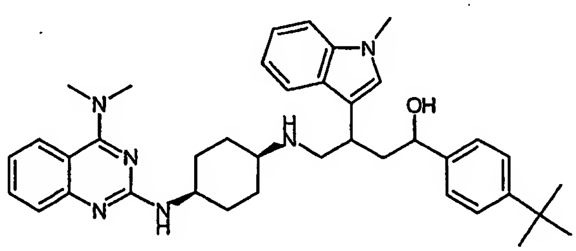
Example No.	Structure	APCI-MS
1447		492 (M + H)
1448		442 (M + H)
1449		516 (M + H)
1450		465 (M + H)
1451		472 (M + H)

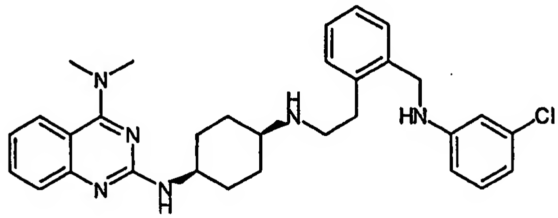
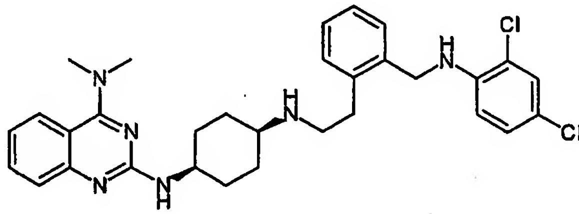
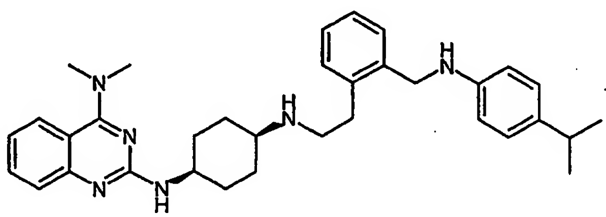
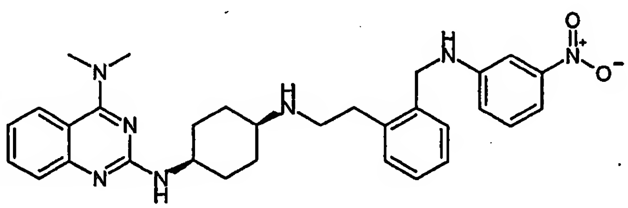
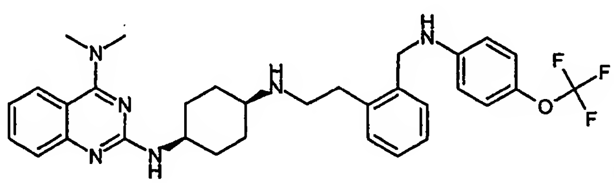
Example No.	Structure	APCI-MS
1452		458 (M + H)
1453		466 (M + H)
1454		450 (M + H)
1455		480 (M + H)
1456		518 (M + H)

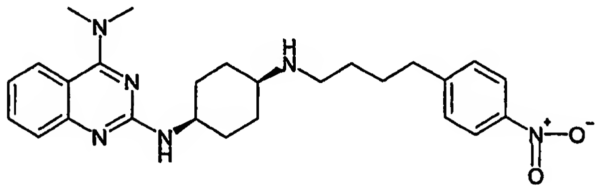
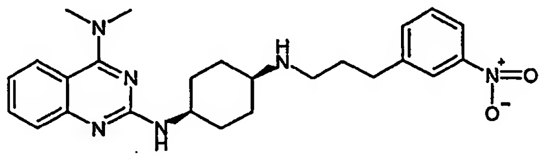
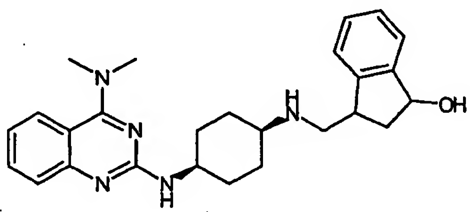
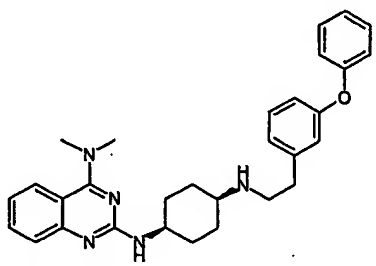
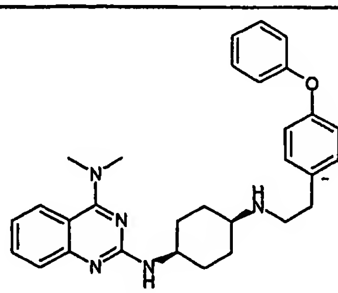
Example No.	Structure	APCI-MS
1457		532 (M + H)
1458		580 (M + H)
1459		452 (M + H)
1460		498 (M + H)
1461		409 (M + H)

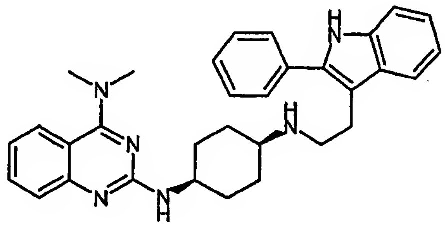
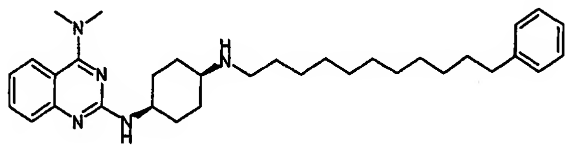
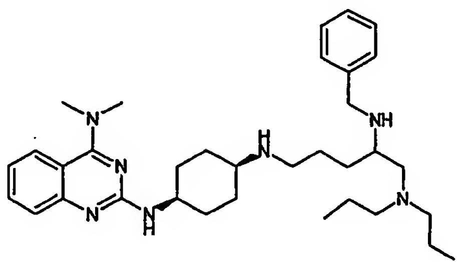
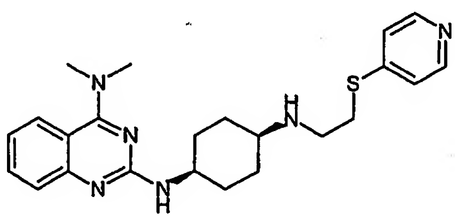
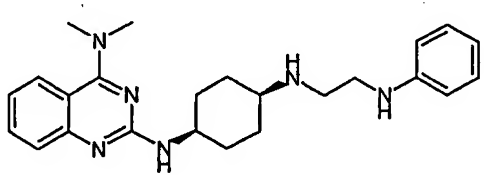
Example No.	Structure	APCI-MS
1462		563 (M + H)
1463		420 (M + H)
1464		535 (M + H)
1465		516 (M + H)
1466		476 (M + H)

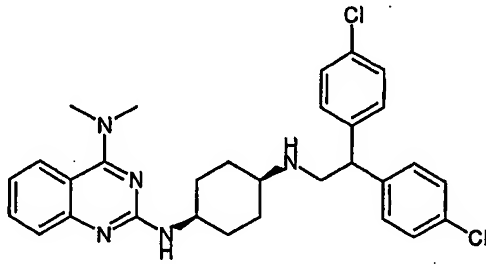
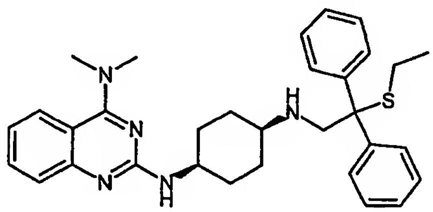
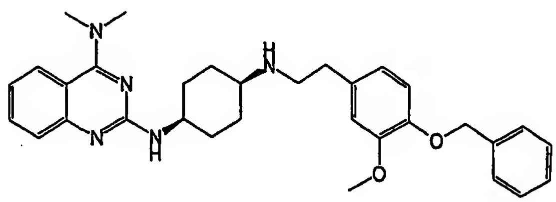
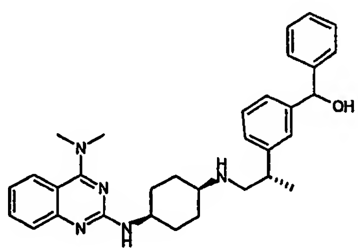
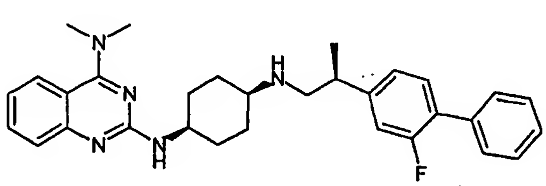
Example No.	Structure	APCI-MS
1467		472 (M + H)
1468		487 (M + H)
1469		548 (M + H)
1470		512 (M + H)
1471		473 (M + H)

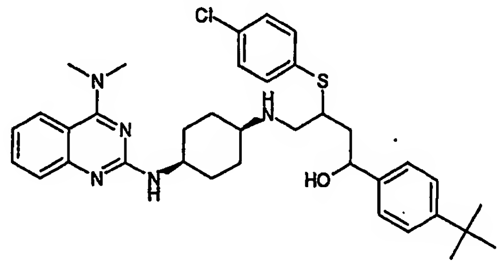
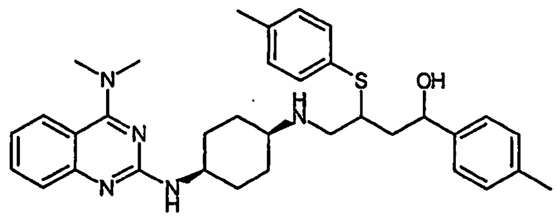
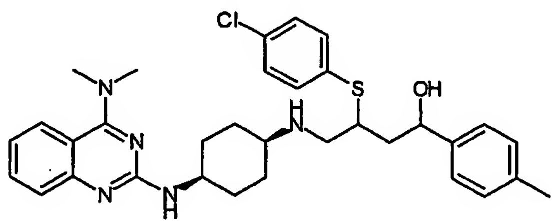
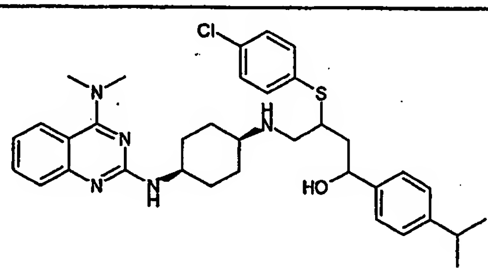
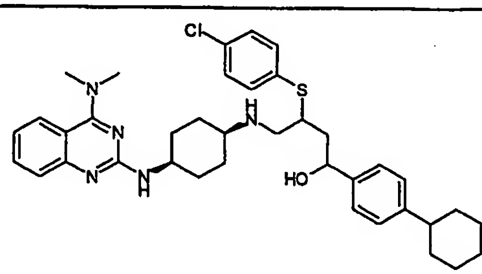
Example No.	Structure	APCI-MS
1472		648 (M + H)
1473		591 (M + H)
1474		645 (M + H)
1475		531 (M + H)
1476		619 (M + H)

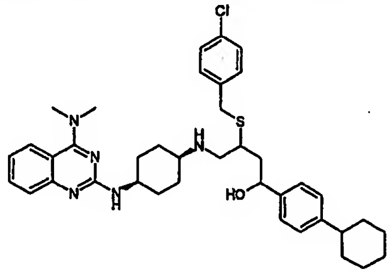
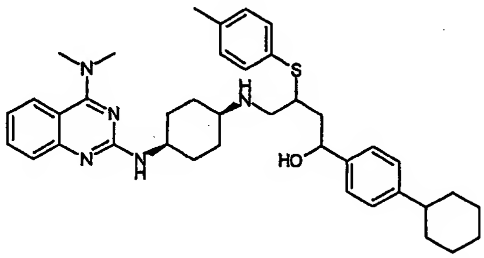
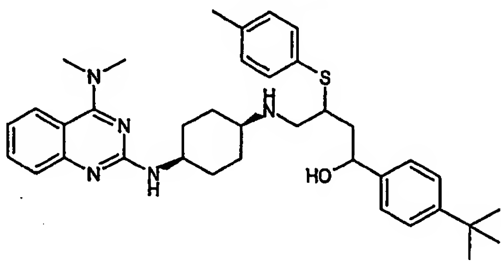
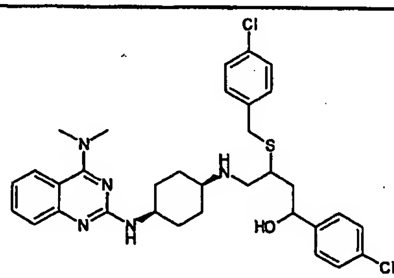
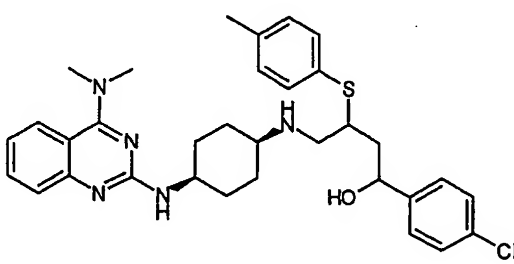
Example No.	Structure	APCI-MS
1477		529 (M + H)
1478		563 (M + H)
1479		537 (M + H)
1480		540 (M + H)
1481		579 (M + H)

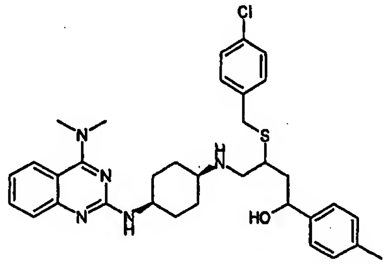
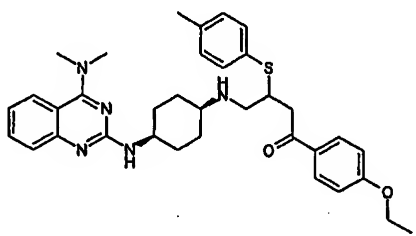
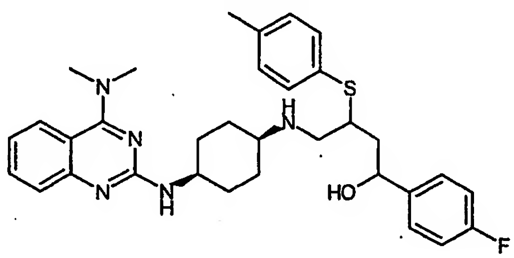
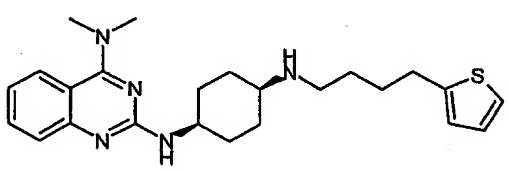
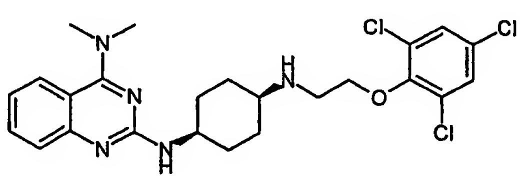
Example No.	Structure	APCI-MS
1482		463 (M + H)
1483		449 (M + H)
1484		432 (M + H)
1485		482 (M + H)
1486		482 (M + H)

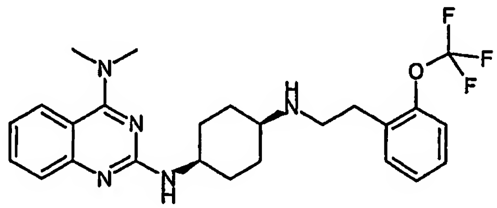
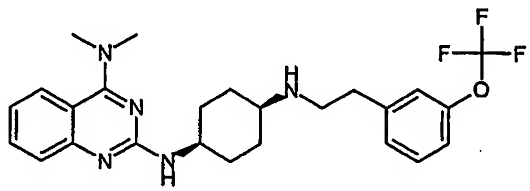
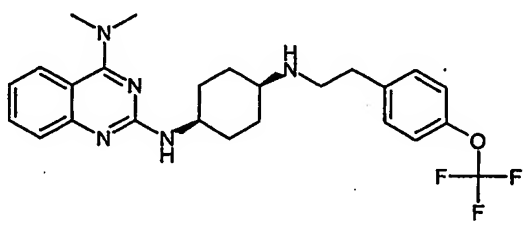
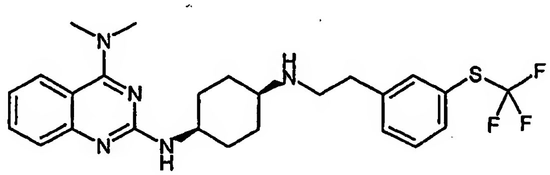
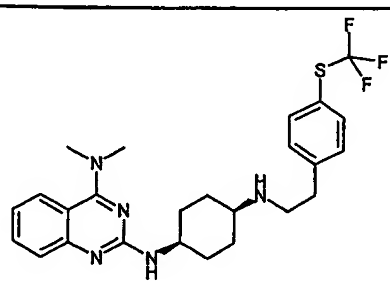
Example No.	Structure	APCI-MS
1487		505 (M + H)
1488		516 (M + H)
1489		560 (M + H)
1490		423 (M + H)
1491		405 (M + H)

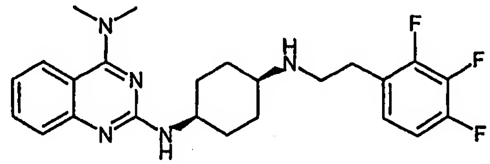
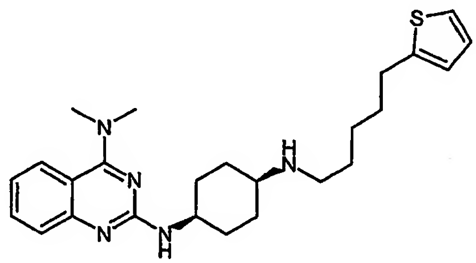
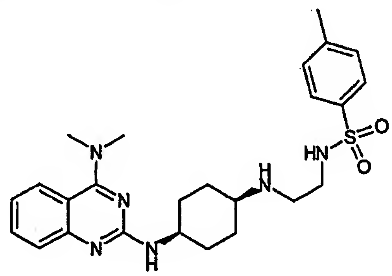
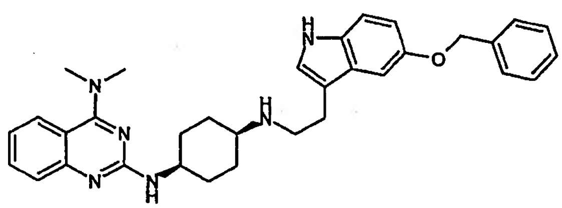
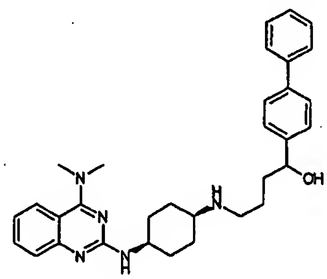
Example No.	Structure	APCI-MS
1492		534 (M + H)
1493		526 (M + H)
1494		526 (M + H)
1495		510 (M + H)
1496		498 (M + H)

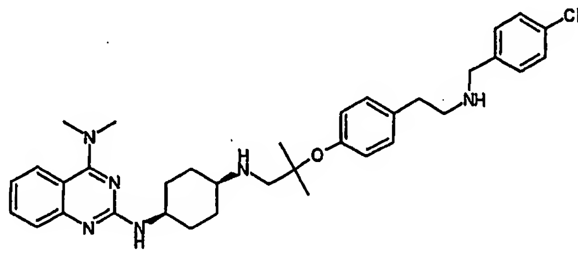
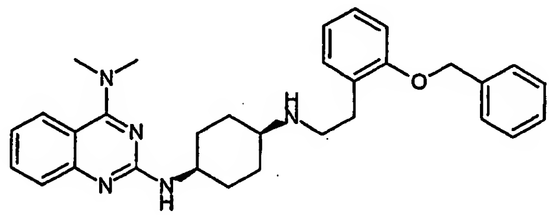
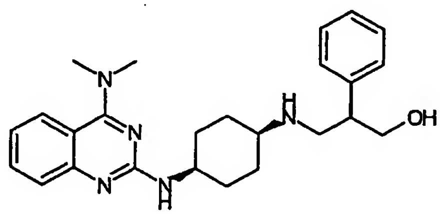
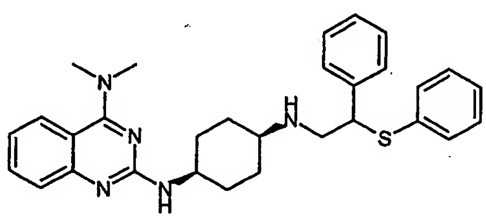
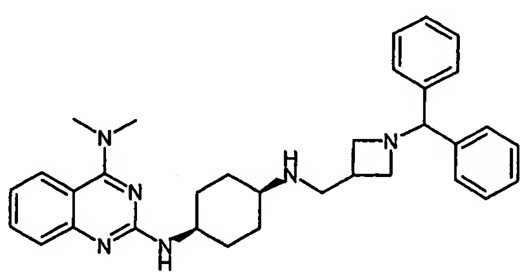
Example No.	Structure	APCI-MS
1497		632 (M + H)
1498		570 (M + H)
1499		590 (M + H)
1500		618 (M + H)
1501		658 (M + H)

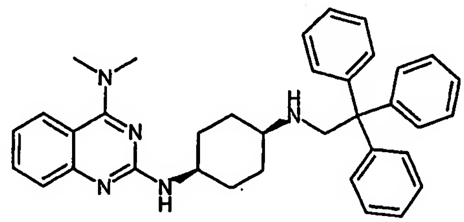
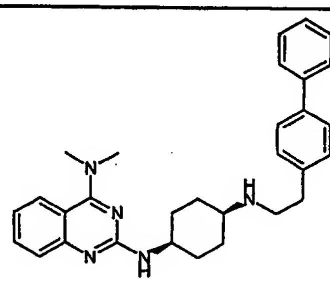
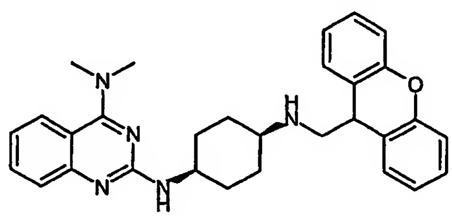
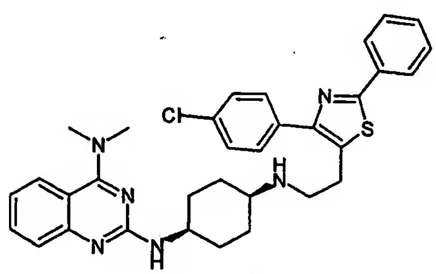
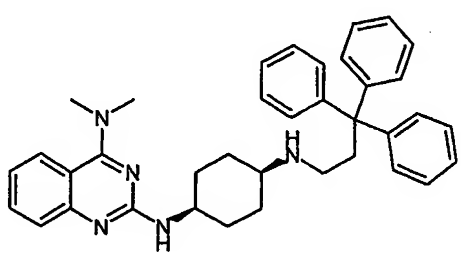
Example No.	Structure	APCI-MS
1502		672 (M + H)
1503		638 (M + H)
1504		612 (M + H)
1505		624 (M + H)
1506		590 (M + H)

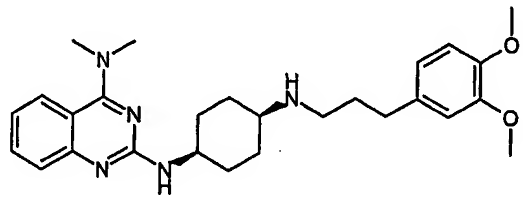
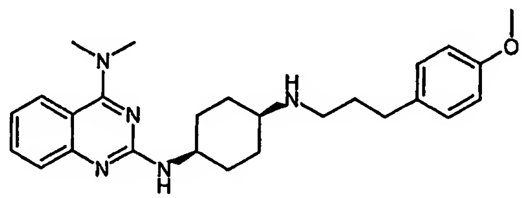
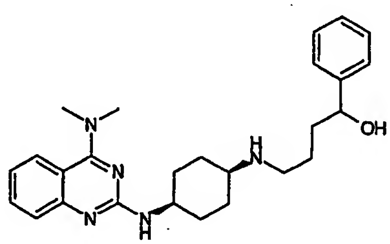
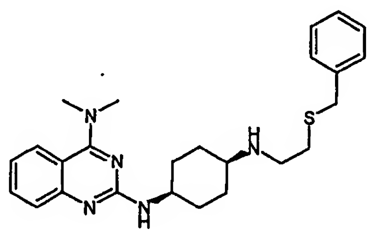
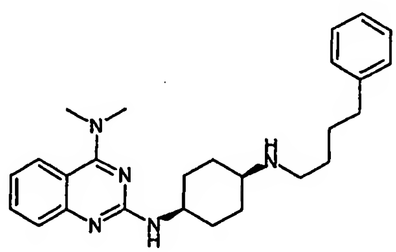
Example No.	Structure	APCI-MS
1507		604 (M + H)
1508		598 (M + H)
1509		574 (M + H)
1510		424 (M + H)
1511		508 (M + H)

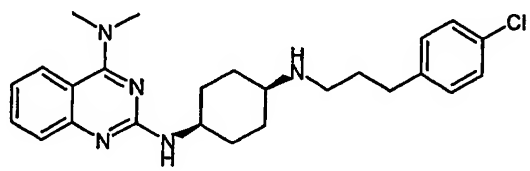
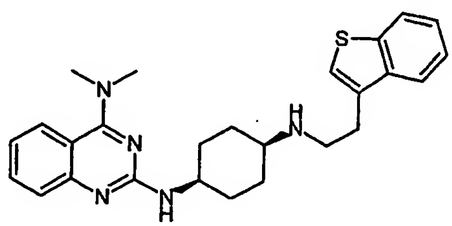
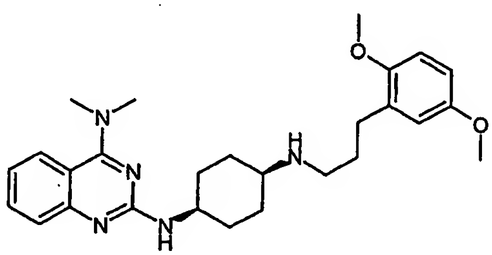
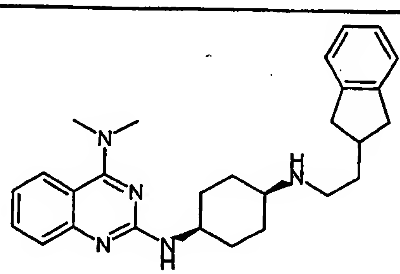
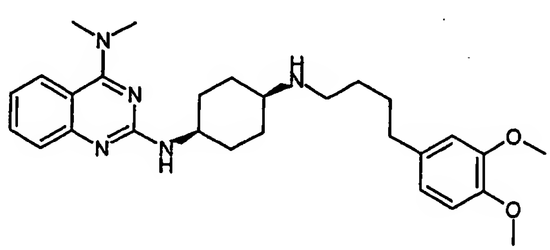
Example No.	Structure	APCI-MS
1512		474 (M + H)
1513		474 (M + H)
1514		474 (M + H)
1515		490 (M + H)
1516		490 (M + H)

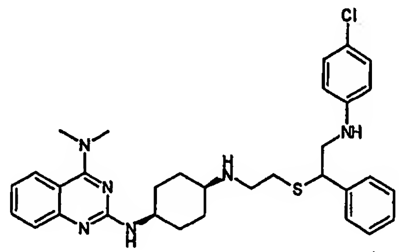
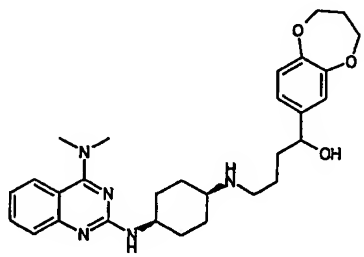
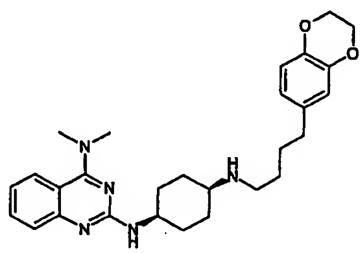
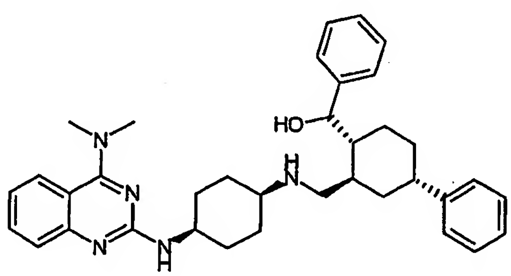
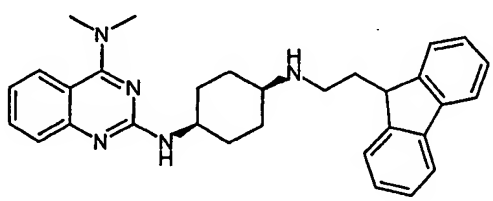
Example No.	Structure	APCI-MS
1517		444 (M + H)
1518		438 (M + H)
1519		483 (M + H)
1520		535 (M + H)
1521		510 (M + H)

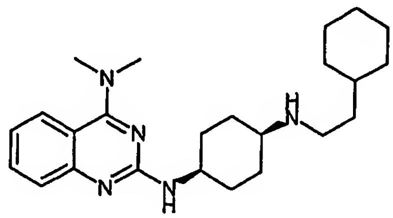
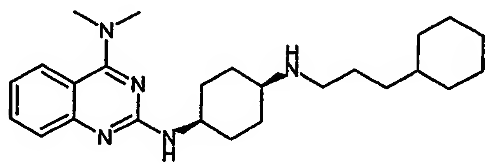
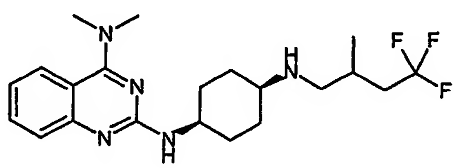
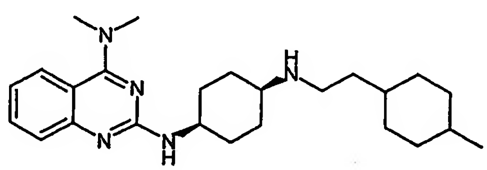
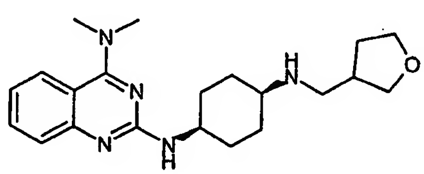
Example No.	Structure	APCI-MS
1522		601 (M + H)
1523		496 (M + H)
1524		420 (M + H)
1525		498 (M + H)
1526		521 (M + H)

Example No.	Structure	APCI-MS
1527		542 (M + H)
1528		466 (M + H)
1529		480 (M + H)
1530		583 (M + H)
1531		556 (M + H)

Example No.	Structure	APCI-MS
1532		464 (M + H)
1533		434 (M + H)
1534		434 (M + H)
1535		436 (M + H)
1536		418 (M + H)

Example No.	Structure	APCI-MS
1537		438 (M + H)
1538		446 (M + H)
1539		464 (M + H)
1540		430 (M + H)
1541		478 (M + H)

Example No.	Structure	APCI-MS
1542		575 (M + H)
1543		506 (M + H)
1544		476 (M + H)
1545		564 (M + H)
1546		478 (M + H)

Example No.	Structure	APCI-MS
1547		396 (M.+ H)
1548		410 (M + H)
1549		410 (M + H)
1550		410 (M + H)
1551		370 (M + H)